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The Psychological Approach to Rheumatism

By J. L. Halliday, M.D.

My thesis is this : *If we omit to include the psychological approach in our investigations, the range of our observations may be too narrow with the result that our action, whether designed for treatment or for prevention, may be ineffective or even harmful.*

In the speaking time at my disposal I am aware that it is not possible to justify this thesis to you. I should however like to interest you and provide something practical, so that you may yourselves begin to include this method of approach in your examination of patients. This may perhaps be accomplished if I illustrate the application of a psychological approach in non-arthritic rheumatism. I may add at this point that the principles of investigation are also applicable to arthritic rheumatism.

The psychological approach refers to a technique of investigating the living person. There are other approaches with which you are more familiar, as for example the structural approach which studies the person in terms of architecture—by anatomy, histology, and pathology. Then there is the physico-chemical approach which studies the person by the techniques of physics and chemistry. And there is the psychological approach which studies the person as an integrated unit. This approach is often neglected but it may be very relevant to our understanding of illness.

Illness is the reaction of a person to something he has met as he grows and moves in time. Illness is a mode of behaviour of a person or a community. It is the person, not the organ, that is ill.

Environment is the name we give to the surrounding of a person at any point in time. We can study the surrounding by applying various techniques and thus split it up into fragments which we call factors. For example we talk of physical factors (trauma, heat, cold, wet) ; of chemical factors such as gases, dust, diet, poisons ; of micro-organic factors, and of psychological factors. By this term we mean those factors which we contact " through the mind ". Although they may not touch us in the physical sense yet they may touch us deeply. Examples are the loss of a beloved person or object, as in bereavement, frustrated career, &c. We react to such psychological factors by emotion.

Illness and the Emotional Reaction

The physiological mechanisms concerned in emotion have been demonstrated in broad outline by recent researches. The body structures involved are the diencephalon, the autonomic nervous system, and the endocrine glands. Anatomically these three structures are related closely ; functionally they may be regarded as three variables, no one of which can be studied in the conscious living person without reference to the other two. If as physiologists we consider that the function of the diencephalon is " sensing and feeling " we are enabled to understand how psychological factors of the environment " touch " the individual at the organs of the special senses and thus bring into action mechanisms which may cause, ultimately, changes in chemistry, secretion, rhythm, muscle tonus, &c. To omit consideration of the diencephalon in considering physiological mechanism is to sin against the light. These mechanisms are a triad, and inferences from observations which are limited to the autonomic and endocrine systems must inevitably be unsatisfactory.

If for any reason an emotional reaction is maintained in its original or modified form, illness may result. Many morbid modes of behaviour are best regarded as emergents of emotional reaction, but when psychological factors are not investigated the significance of these disorders remains hidden under such labels as gastritis, gastroptosis, colitis, tachycardia, angina innocens, asthma, recurring bronchitis, debility, anæmia, rheumatism, &c. In such circumstances the patient remains "a case" which requires appropriate treatment, e.g. alkaline powders for gastritis, an abdominal belt for gastroptosis, sedatives and graduated exercises for simple tachycardia, expectorants and nasal operations for bronchitis, and so on. Omission to consider the psychological approach at the beginning of illnesses labelled by such terms may result in chronic invalidism, after the failure of endless "appropriate lines of treatment". I do not wish to be misunderstood. All factors of the environment are lawful for investigation but all are not relevant.

Elementary Psychological Technique

If we do not search for psychological factors we fail to discover them. Also when we do search for them we must do so in the proper way. In other words we must be willing to admit that there is an appropriate technique for each method of approach to the environment. For example, if a doctor using the bacteriological approach stains a patient's sputum with methylene blue and reports that no tubercle bacilli are present we must agree that this negative conclusion is of no value, because the technique which he employed was inappropriate. In the same way we must not be surprised if we discover no psychological factors when we examine the patient in the wrong way as, for example, in the presence of other persons, or if we shout at him or announce that there is nothing the matter with him, or act in a hurried or highly important or fussy fashion.

There is nothing mysterious in the appropriate technique. It demands consideration of the patient, not as a case but as a person. It also requires a knowledge of certain features of illness which emerges from emotional reaction, namely (1) the innocence of the patient, (2) his increased suggestibility, and (3) the unconscious purpose of his behaviour, i.e. the patient in his heart of hearts has a motive for being ill and may not be prepared to face the consequences of recovery. These features were discussed in a previous paper (1937*a*).

The Application of the Approach to Non-Arthritic Rheumatism

This section is based on observations made on patients labelled "rheumatism" who complained, *inter alia*, of pain and stiffness, but who on examination presented no evidence of obvious structural change. The patients were labelled by such terms as muscular rheumatism, fibrositis, lumbago, sciatica, neuritis, &c. It describes the application of the psychological approach to these patients and shows how their modes of behaviour would have been labelled more accurately by such terms as psychoneurotic anxiety states, hysteria, or sometimes psychotic depression.

The Illness in Time

A patient who develops "rheumatism" in the course of emotional reaction tends to date the onset of his illness to the time when the rheumatic symptoms (pain, stiffness, swelling) first appeared. His preceding disturbances may have been very definite and very severe, and may have included mental symptoms—such as depression, lack of concentration, withdrawal of interest, feelings of futility and unreality, as well as physical symptoms—such as weakness and exhaustion, insomnia, palpitation, lack of appetite, abdominal discomfort, numbness, tingling, transient losses of power, &c. But an account of these is not usually volunteered spontaneously. The patient's consciousness is dominated by his rheumatism and the preceding disturbances are suppressed. When we investigate the story of a patient's rheumatism we must direct

our inquiries, therefore, to two points in time: not only to the date of onset of the rheumatism but also to the date of onset of the various symptoms which preceded it and may still accompany it. Sometimes we find that there is a lightening of the mental symptoms when the bodily symptom appears: psychologists describe this phenomenon by saying that the emotion has been *converted* into the bodily symptom.

Features of the Mode of Behaviour

Physical examination.—During physical examination, apart from noting what structural and other changes are present, consideration should always be given to the patient's face and manner. From these much may be learned about the kind of person and the things he has met. Some doctors, however, seem very insensitive to this aspect of a patient.

Facial expressions which give us a hint that the illness may have emerged from emotional reaction may be divided into two extreme groups—the anxious, and the detached. The anxious face may be described as strained, tired, worried, or hunted: it is associated often with fine tremors of the outstretched fingers—which are detected readily against a background of newspaper print; with tachycardia or visceroptosis. At the other extreme the detached face may be restful, placid, complacent, smiling, or "spiritual"—in short pathologically free from anxiety. It is associated sometimes with marked thudding of the aorta in the epigastrium. Detachment of face and manner is sometimes called "la belle indifférence" and usually indicates that the disturbing emotions, and sometimes also the situation which provoked them, have become dissociated from the consciousness of the patient.

Psychological examination.—Much can be learned about a patient when we ask the preliminary questions which deal with age, occupation, &c. Of particular interest are the patients who "protest too much" and keep repeating such phrases as "I was never the one to give in, doctor," "It doesn't pay *me* to be ill"; "I would work if I could", &c. Henley in his poem "Invictus" describes this attitude well:—

> "In the fell clutch of circumstance
> I have not winced nor cried aloud;
> Under the bludgeonings of chance
> My head is bloody, but unbowed."

"Invictus" patients who keep repeating: "I was never the one to give in", very frequently complain of stiffness of the neck or back, or of other pains, spasms, losses of power, &c., with no discoverable organic basis.

Characteristics of the Person (the First Field of Ætiological Discourse)

What kind of person develops rheumatism as an emergent from emotional reaction? Little is known about their characteristics. Items noted among insured persons include the following:—

(1) *Age and sex.*—All ages may be affected. The sexes suffer in about equal proportions. There is a certain amount of evidence to indicate that the maximum age distribution of onset is about 35 to 45 years. In females with the characteristic of "menopause", fibro-fatty thickenings, in addition to pain and stiffness, seem especially liable to appear as emergents of emotional reaction; these are labelled by such terms as fibrositis, panniculitis, peri-arthritis, and endocrine dysfunction.

(2) *Marital status, &c.*—Rheumatism, especially in its "neuritic" manifestations, is especially frequent in (*a*) widows and widowers, (*b*) in married persons who live apart, whether from disagreement, desertion, or illness, and (*c*) in persons who live alone or who feel that they are living alone.

(3) *History of previous illnesses.*—Many of the patients have on previous occasions responded to life's stresses by illnesses which emerged from emotional reaction. An inventory of such illnesses includes such terms as anæmia, headache, recurring colds, bronchitis, gastritis, cardiac debility, nervous breakdown.

Note.—The symptom of pallor, which is very common, is not necessarily an

indication of anæmia. Among insured persons its presence is more often associated with an anxiety state than with deficiency in hæmoglobin or blood-cells.

(4) *Occupation.*—Certain occupations seem more liable than others to be associated with psychoneurotic illness. In males may be instanced miners, workers at heights (slaters, steel erectors, &c.), and clergymen; in females, typists, housekeepers, cleaners, nurses, and piece-workers; in both sexes, teachers and canvassers, travelling agents who work "on commission", and those in sheltered clerical occupations in which the instinct of creation is continuously thwarted. I have an impression that persons who in the past have undergone a rapid "religious" conversion are liable to attacks of severe pain, commonly called rheumatic.

The Environmental Factors Encountered (the Second Field of Ætiological Discourse)

In rheumatism which emerges from emotional reaction, psychological factors which are common are those which entail deprivation or loss of a loved object, whether person, career, or material goods.

Psychological Mechanisms (the Third Field of Ætiological Discourse)

When a particular psychological factor touches a particular kind of person through the special senses it sets into action certain mechanisms which may ultimately bring about a particular mode of behaviour. The question—Why does a person take ill in the way he does?—completes our understanding of any illness. The mechanisms involved may be studied by various techniques, e.g. structural, chemical, physical, psychological, &c. Psychological mechanisms which determine the nature of a person's reaction include the following: Inherited patterns of behaviour; acquired bodily inferiority; fears and knowledge of disease; and symbolism.

Inherited patterns of behaviour.—Inherited patterns of behaviour may play a part in determining the nature of a person's reaction. It is a common belief that one family tends to be "highly strung", another "chesty", another to have "weak stomachs". The influence of inheritance has been carefully worked out in some illnesses such as asthma, but this illness happens to be particularly suitable for such studies because it is both visible and audible, and therefore easily noted by relatives. Many modes of behaviour are invisible and silent, and studies of rheumatism, a vague term, are particularly uncertain. Moreover it is probable that most people have suffered on occasion from pain and stiffness.

Acquired bodily inferiority.—During emotional reaction, pains and other symptoms tend to be located in parts of the body which have been affected previously by operation, injury, or "disease". An example may be cited.

Example No. 1

Date of examination, April. On the sick list from February 10 with a diagnosis of right-sided pleurodynia.

Features of the mode of behaviour. No evidence of abnormality of lungs or of chest wall. Anxious expression; tachycardia; abdominal pulsation; brisk knee-jerks.

What kind of person was this? A slater, aged 42; married, but devoted to his mother. History of right-sided pneumonia seven years before.

Why did he become ill when he did, viz. in February? In January his younger brother, who was the support of his parents, ran away with a married woman. The patient wished to call in the police to search for him, but his parents refused. There was a family quarrel, his mother stating that the young brother was less able to support his parents than the patient. The patient replied that he would never put his foot again over his mother's doorstep. After this he spent sleepless nights, went off his food, &c., and early in February he developed pain in his right chest and became afraid that he would develop pneumonia again.

Why did he become ill in the way he did, viz. with emotional reaction and later right-sided chest pain? His mode of behaviour was a response to psychological factors, and a mechanism which determined the site of his pain was acquired bodily inferiority.

Previous action. He had received poultices, belladonna plaster, and later, massage, without benefit.

Action based on the observations. The telling of his story released much pent-up emotion. He was reassured about the absence of pneumonia and he came to understand the meaning of his pain. He decided to re-visit his mother and to resume work.

Comment.—It seems reasonable to conclude that this man's incapacity of two months' duration was not inevitable. The failure to prevent it lay—

(1) In the omission during physical examination to pay attention to the patient's facial expression and behaviour—in other words, nobody " looked upon the man " ; (2) in the lack of knowledge of the questions of ætiology (in other words, the examiner's attention was focused on securing a label and not on ascertaining cause).

After negative bodily examination the order of approach should have been : " Here is an anxious-looking man. A slater—as bad as a miner. I wonder what the fellow met—probably an accident to a workmate. No ; apparently no accidents ". . . . Then later : " The balance of probability is in favour of a label of psychoneurosis. The mode of behaviour is of the nature that is associated with reaction to psychological factors. Moreover this interpretation covers each of the fields of discourse. It fits and it works, whereas the ' pleurodynia ' interpretation does not fit and therefore cannot possibly work ".

Fears and knowledge of disease.—It is not uncommon for medical students or nurses in the course of their studies, to rush to one of their teachers in the fear or belief that they have developed some illness of a serious nature. Usually this happens during a time of anxiety, as for example before an examination. The medical student as a rule states what is in his mind, but usually the nurse is silent. A little knowledge of medicine may be highly dangerous. Among the general population of to-day, health lectures, newspaper articles on disease, magazines devoted to the body, medical dictionaries, &c., are part of the everyday environment, and by these means the instinct of bodily self-preservation is being constantly " tickled ". As a result, when a person develops emotional reaction—and a feature of this state is increased suggestibility—he may accept from his " knowledge of disease " the idea that he is the victim of a grave illness and the nature of the illness so selected may determine in part the nature of his bodily symptoms.

Of deeper importance, however, is the mechanism known as " identification ", a word which refers to the tendency of an individual during emotional reaction to behave in the same way as those round about him, especially those whom he loves. A good example, although a rare one, of such identification is the " morning sickness " of a young husband when his wife becomes pregnant for the first time. The phenomena of identification are not uncommon after bereavement. When an individual loses a loved person—parent, relative, child, marital partner, friend, or work-mate—he may develop, during the emotional reaction of grief, symptoms similar to those of the loved one. Pains diagnosed as rheumatic may sometimes develop in this way. Spiritualists explain these identifications following bereavement by saying that the patient is " possessed " by the spirit of the departed. The subject of identification is a fascinating one and its bearings on practical aspects of medicine, such as hospitalization, are not yet explored.

Examination of any patient with rheumatism is incomplete and the inferences made may be misleading if investigation is not directed to illness or death of loved persons ; the nature of such illness ; and the knowledge, fears, and beliefs of the patient concerning his own illness.

The following example may be cited :—

EXAMPLE NO. 2

Date of examination, December. On sick list from October 10 with a diagnosis of "headache".

Features of the mode of behaviour. Placid and smiling ; taches of neck and chest ; slight

tremors. Specialist's examination of eyes, throat and nose negative. X-ray examination of skull negative.

What kind of person was this? A domestic servant, aged 32; single; subservient to an overwhelming mother; of stout build. Previous illnesses include "lumbago", and "anæmia and debility".

Why did she become ill when she did, namely in October? In May her aunt who lived near her mother was diagnosed to have cerebral tumour. Operation was performed, but no hope of recovery was given. In August the patient's aunt left hospital and returned home. Every Thursday evening the patient visited her aunt who suffered from very severe frontal headaches, and also had by this time developed paralysis of the left arm and leg. Early in September she died. The weekly visits had affected the patient very much and she always left her aunt feeling very depressed. Further, she did not like her situation—which she had entered in May—"it was too heavy". She became weak, could not eat and felt her heart beating. Frontal headaches began soon after her aunt's death, and also about this time she began to wake up during the night to find that she had lost the power of her left arm and leg. She told her mother about the headaches and the mother said she was probably going the same way as her aunt. The patient was put on the sick list and sent to the out-patient department of a hospital where, after a thorough physical examination, she was labelled—"headaches due to constipation".

Why did she become ill in the way she did, viz. with frontal headache and nocturnal paresis? The mechanisms involved were "fear, and knowledge of disease" with possibly identification. The fears were increased by the suggestion of her mother, and numerous examinations at hospital omitting, however, the psychological approach served to maintain them.

Comment.—This is a good example of the effect of failing to ascertain a recent bereavement, its nature, and the knowledge and fears of the patient concerning her illness.

Symbolism.—Darwin (1873) used the term "expressive action" to denote the movements, gestures, and attitudes from which the existence of an underlying emotional state may be inferred. Thus, "an indignant man who resents and will not submit to some injury, holds his head erect, squares his shoulders, and expands his chest". In hatred and anger, "the body is commonly held erect ready for instant action but sometimes it is bent forward towards the offending person, with the limbs more or less rigid. Such gestures as raising of the arms, with the fists clenched as if to strike the offender, are common. The desire, indeed, to strike often becomes so intolerably strong that inanimate objects are struck or dashed to the ground". Darwin concluded that such movements of expression "*reveal the thoughts of others more truly than do words which may be falsified*".

The word "symbol" is now employed to describe anything that stands for or represents a mental experience. In this sense Darwin's "expressive actions" are bodily symbols. (Other aspects of symbolism were discussed in my previous papers on rheumatism and asthma 1937b.) Symptoms often called rheumatic (pains, rigidity, limitation of movement) may sometimes represent or symbolize deep-seated emotional attitudes. The following are examples:—

(1) Pain and stiffness which are generalized—either wandering or "all over" may mean: *My feelings are hurt. Life has pained me. I feel sore about things and I think them stiff.*

(2) Pain and stiffness in the neck, between the upper scapulæ or in the lumbar spine—associated with limitation of movement, especially flexion—may mean: *I am refusing to accept; I will neither bow nor bend; I resent this person and/or this situation; I am obstinate and stiff-necked.*

(3) Pain and stiffness of the knees with difficulty in bending may be associated with a deep-seated attitude of resentment and may mean: *I will not go down on my knees, neither will I beg nor pray for help.* Sometimes the complaint of inability to bend is preceded by that of inability to rise from the kneeling position. This may originate at a time when circumstances (domestic and financial) seem overwhelming,

and it signifies : *I feel I shall never get on my feet again.* Ray (1929) notes that he has seen patients with non-arthritic peri-arthritis (mostly affecting the knees) which was " undoubtedly due to business worry and domestic troubles ". So long as the worry prevailed, physical treatment had very little effect, but " immediately the cause of anxiety was removed, all the symptoms disappeared almost like magic ".

(4) Pain and stiffness of both arms with inability to raise them and with attacks of loss of power may be associated with hatred of a person and a desire to attack him, but the impulse is repressed. The meaning of this " neuritis " of both arms may be : *I hate him ; I want to raise my hands to him, but—I can't.*

(5) Pain over the top of the left shoulder and on the outer side of the upper third or half of the left arm may emerge for the first time during an emotional reaction following bereavement or mischance. These pains, which may begin near the mid-point of the spine of the scapula, may be very severe and are often accompanied by cramps, numbness, pricklings, losses of power, and later with wasting. This " neuritis " of the left shoulder and arm is very definite, is not uncommon, and is usually treated—unsuccessfully—with massage. Its symbolism is, *inter alia*, a " sinister " one, and may often be interpreted as : *I am unlucky ; I have met with misfortune ; I am abandoned.* (In left-handed people the corresponding symptom is found on the right side, but a similar neuritis of the right arm may occur in right-handed persons, especially perhaps in women, as a response to such circumstances as the loss of the bread-winner and the need to begin to earn an independent livelihood.)

A sinister symbolism is also found in certain examples of left-sided chest pain. I have noted that pain (or burning or skin irritation) in the region of the 12th left rib, may occur after the loss or leaving of a beloved married partner. The association may be a chance one but it is surprising how often it seems to fit. This type of " pleurodynia " may perhaps be related in some roundabout way to the mythical story of the formation of Eve from Adam's rib. Pain in the leg in the region of the hip-joint, especially the left one, sometimes occurs after deprivations which may include the death or departure of a beloved child. The symbolism involved here may have reference to a bud ; an out-growth ; an offspring ; a branch or a limb. In common language we talk of a branch of a noble house, a limb of Satan, &c.

It is evident that the symbolism of these pains needs further investigation. The predominance of the left side is however clear, and it is helpful to regard it as associated with ill-luck, loss, and mischance. In folklore and etymology the left side is associated with ideas relating to evil, mystery, femaleness, &c.

To sum up : Certain symptoms—commonly called rheumatic—may be symbols of deep-seated emotional experiences. These symptoms may be motor (e.g. cramp, loss of power, limitation of movement), and sensory (e.g. aches and pains, as well as numbness, tingling, and burning).

To avoid misconception about symbolism certain points need emphasis :—

(*a*) The translations into words of certain rheumatic symptoms are not fanciful —not mere word-play and punning. They are fair inferences from observation over a large number of patients whose rheumatism emerged from emotional reaction. In the first instance they were made from clinical investigation and later they were found to be related to knowledge gained in other sciences—folk-lore, etymology, and the " expression of the emotions ". In other words, the interpretations of the symptoms are inductions from facts—not deductions from any generalization.

(*b*) A knowledge of symbolism is of practical value and serves to remind us not only that rheumatism (and other complaints) may have emerged from an emotional reaction, but also that this reaction may have been of a special kind. Thus rheumatism is commonly associated with an emotional attitude which may be described as one of aggression. Sometimes the aggression is negative and takes the form of resentment, refusal, pride, &c. (*see* examples of symbolism Nos. 1, 2, and 3) ; sometimes in the forms of hate and hostility it is very positive (*see* example No. 4). Rheumatic

symptoms are common after grief, the response to the loss of a beloved person or object (*see* example No. 5). Grief, however, is seldom "pure". It is usually associated with resentment as well as with fear and guilt. With further and deeper research these bodily symbols may be fitted with a more precise interpretation. In the meantime if we appreciate that rheumatic symptoms may also be symbols we are enabled to direct our inquiries quickly to what may be relevant in ætiology and proper for treatment.

(*c*) Failure to decipher a symptom which may be symbolic is often associated with failure to make allowance for the "innocence" of the patient. Darwin's observation, quoted on p. 6, showed great perspicacity. Time and again a patient who a few minutes before had asserted that he had no worry, no upsets, no mental stresses, and never had a care in the world, will announce that he might as well tell the truth, and his tale will indicate how exactly the bodily symptoms symbolized his mental experiences.

NOTE.—The symbols which we have been discussing may be described as phylo-genetic. They are collective, i.e. common to all men, and are associated with the evolution—physical, mental and cultural—of the human species. Symptoms determined by the mechanisms of "acquired inferiority" and of "knowledge and fear of disease" may also be regarded as symbols, and because their meaning is to be found in the life of the individual—not of the species—they are called onto-genetic symbols. From this point of view a symptom may be symbolic in two senses—collective and personal—and may be interpreted both phylo-genetically and onto-genetically.

NOTE ON FIBROSITIS

I did not see these patients at the beginning of their illness and the question may properly be asked: "Although nothing was evident at your examination, did they have fibrositis when they first began to complain of pain and stiffness?" Reports available from their practitioners often stated that they did have fibrositis. This raises several interesting issues. For example, it is easy to be deceived in the detection by palpation of small nodules and fibrositic thickenings. Moreover, the examiner does not always guard against the possible effect of his remarks and actions on the patient. When we recall that patients suffering from psycho-neurotic illness may be highly suggestible, we are able to understand how remarks such as "Do you feel that?", especially if repeated and if accompanied by increasing digital pressure, may rapidly induce very painful sensations, with the result that when the patient winces or screams, the examining doctor may congratulate himself on having demonstrated the location of a nodule. On the other hand, by suggestion which is sedative, either by word (e.g. "You don't feel that, do you?") or by deed (e.g. the various forms of physical therapy) a painful area may become less painful or completely anæsthetic.

Another problem is this: Does objectively demonstrable fibrositis make its first appearance as an emergent of emotional reaction? So far as I can discover no systematic investigation has been directed towards this. Copeman (1935) makes the significant statement that in almost every patient there will be found, if sought for, a longer or shorter period of considerable antecedent overwork, mental worry, or anxiety. He adds: "This is important, as it should indicate therapeutically both the danger of over-treatment and the need to prescribe a suitable holiday when the acute stage is over". It is evident, however, that he has not exhausted the implications of his findings, which, if viewed with psychological understanding, should provide a guidance to therapeutic action even more effective than the routine recommendation of a holiday. In the literature we may also read about patients who developed fibrositis after severe emotional stress, who showed little improvement during active physical treatment, but who began to recover when the life situation became less pressing (e.g. Gordon, 1936). Among insured persons I sometimes see patients with very definite fibrositic nodules present at the time of examination who, however, had

made no complaint of pain or stiffness until after severe or prolonged emotional reaction. Observations such as the foregoing may be related to what is known or inferred about the physical mechanism of fibrositis. This is said to involve the endocrine glands and the autonomic nervous system (Copeman, 1936).

There is need for further investigation not only into the relationship of fibrositis to emotional reaction but also into the incidence of nodules and fibrositic thickenings in the healthy (i.e. the non-complaining and non-incapacitated) population at the various age and sex groups.

Conclusion

I have attempted to show that the psychological approach to rheumatism is neither muddle-headed nor mystical; it is scientific and practical. Its employment indicates that we are beginning not to lose, but to achieve, a sense of proportion and perspective. By the use of a simple psychological technique, observations may be made which are relevant to the ætiology, treatment, and prevention of much incapacitating illness which is labelled in practice and in official statistics by the comprehensive term "non-arthritic rheumatism". The application of this approach is also relevant in chronic arthritis when this is not a response to defined infection. Only reasons of space prevent its consideration here. All observers who have used this method of approach in a clear-headed fashion are agreed that imperfections in our knowledge and treatment are related, *inter alia*, to our neglect to apply this technique of approach from the onset of the illness. In the absence of this method of investigation our examination of a patient may be incomplete, with the result that our treatment may be ineffective or even harmful. Moreover any scheme of research into rheumatism which omits this method of investigation in its inquiries is founded on an imperfect appreciation of the meaning of scientific method and must therefore end in frustration, either partial or complete. Further, while this neglect continues, the accurate assessment of various forms of physiotherapy will be impossible of appraisement. Also quackery, whether witting or unwitting, will continue apparently to succeed, whereas orthodox medicine will continue apparently to fail.

These things will, however, neither be believed nor accepted until students of rheumatism overcome their resistance and make the necessary effort—and it demands an effort—to become acquainted with a simple psychological technique and apply it for themselves in their daily practice. Until then the meaning of much incapacitating illness called rheumatism will be misunderstood; faulty inferences will continue to be made (in the name of scientific medicine) from a too-narrow range of observations; and, inevitably, action both in treatment and prevention will fail to be properly effective.

In the words of Fougasse: *You have been warned!*

References

Copeman, W. S. C. (1935), "The Treatment of Rheumatism in General Practice", London, 2nd Ed., pp. 18, 204.
Id. (1936), *J.A.M.A.*, **107**, No. 16, 1295.
Darwin, C. (1872), "The Expression of the Emotions", London.
Gordon, R. G. (1936), *Brit. M. J.* (ii), 1244.
Halliday, J. L. (1937), *Brit. M. J.* (i), 213, 364.
Id. (1937b), *Brit. J. Med. Psych.*, **17** (i), 1.
Ray, M. B. (1927), "Rheumatic Diseases", London, pp. 43, 64, 69.
Id. (1934), "Rheumatism in General Practice", London, pp. 13, 120, 396.

Discussion.—Dr. R. G. Gordon: Dr. Halliday has discussed the psychological approach to certain conditions in which as he said no physical changes could be found. In other words, these were cases of hysteria or other form of psychoneurosis and not truly rheumatic at all.

I wish to discuss the psychological approach to those cases which are properly sent to us as rheumatic, but in which there is a definite psychological factor without the removal of which no satisfactory cure can be obtained. The most obvious type under this heading is

the compensation case in which, say, a workman has received an injury to his back with deep bruising, resulting in very real fibrositis. If, however, he is an elderly man he may feel that, meagre as the compensation is, it is better than nothing and that, if he gives it up, he may never get another job which he is able to do. He is therefore, in a sense, using his illness to avoid a more satisfactory adjustment to life. Before he can be cured it is necessary to use psychotherapy, which may take the form of a just settlement of his claim in a lump sum, in order to induce him to face up to life and work once more. Then, and only then, will the fibrositis be satisfactorily treated.

There are, however, other people who use chronic diseases and perhaps especially the rheumatic diseases, owing to their rather uncertain signs and symptoms, to avoid unpleasant adjustments to life. One may mention the elderly young woman, whose love affairs have turned out badly, in whose case the emotional disturbances may themselves help to initiate the rheumatic changes. Here psychotherapy must persuade her either that there are as good fish in the sea as ever came out of it, or that she must face up to a state of single blessedness. Then only we may be able to deal with the rheumatism.

The most important group, however, and the most difficult to deal with, are the middle-aged and elderly, who have some rheumatic trouble and on account of this, or for other reasons, feel that life has lost its savour. We all know the hunting man with a mild osteo-arthritis of the hip who goes about complaining and grumbling far more than others with a more severe degree of the trouble, because he feels that if he can no longer hunt he might just as well be dead. It is not easy to persuade such a man to face the future cheerfully, because, as a rule, he has no suitable sedentary hobbies.

Sometimes the profession is not altogether guiltless of intensifying the depression of these middle-aged people. How many come for treatment armed with a skiagram of their lumbar spine in which it has been pointed out to them that osteophytes are present, indicating a spinal arthritis! Such long Greek names frighten them and they are not to know that practically everyone over 50 whose back has ever been subjected to strain possesses such osteophytes. Once they can be persuaded that there is nothing very dreadful the matter with them, they cheerfully accept treatment for the fibrositis—which is probably really responsible for the troubles of which they complain—and go on with their lives cheerfully and usefully.

It does not always follow that psychotherapy should precede physical treatment when dealing with these cases. The institution of definite physical treatment for a definite physical condition often gives the patient confidence and allows the physician to obtain the necessary rapport or transference to enable him to practise psychotherapy successfully. When and how this latter treatment is to be introduced in any given case is a problem which the wisdom of the physician will be called upon to solve.

Apart from these psychological concomitants of rheumatic disease, psychogenic factors may actually be causal in the production of rheumatism. Many authorities have noted emotional shock or strain as immediate precursors of rheumatoid arthritis. Nursing sick relatives, the sudden loss of a beloved person, or even personal psychic traumata such as assault or accident, may frequently be found. In my experience, when acute severe fibrositis appears in young subjects, there is practically always a history of emotional strain or stress. Such a condition is common in overworked school-teachers, especially if they are of the neurotic type, and I have had as patients young women whose husbands have followed some dangerous occupation such as aviation.

Therefore when we are treating people in ill-health we have got to consider more than one factor. In the case of rheumatic diseases we have probably got to keep in mind degenerative changes, infection and emotional disturbance and we cannot afford to neglect a thorough search for all three.

Degenerations will be indicated by arteriosclerosis and signs of cardio-renal disease. Infections are nowadays indicated by blood-counts and examinations of the sedimentation rate, but we must also look for positive indications of emotional disturbance. We must pay close attention to the patient's general appearance and attitude to life. Is he anxious, frightened, or depressed? If so, it is our business to find out why. A study of sleep and dreams is often useful, both as indicating trouble and giving us a line towards correct treatment.

Even in cases which seem to be obviously infectious in nature we must not forget the soil on which the infection finds lodgment, and this may require treatment just as much as does the infection itself. When we investigate this our first step is generally to discover

endocrine anomalies or disturbances in the balance of the autonomic system with resultant vascular and biochemical changes.

It may not, however, be sufficient to treat these empirically, for they, in turn, may well be due to emotional disturbances. The seat of the emotional life is largely the thalamus, and here we find a very close relationship with the hypothalamus, which is the headquarters of the autonomic system, and therefore largely responsible for vascular, biochemical, and endocrine regularity.

In the treatment of rheumatic disease we are unfortunately none too successful, and therefore we cannot afford to neglect any method of approach, and of the possible methods the psychological approach is by no means the least important. We must see to it that our patients are emotionally at peace, and that is one of the reasons why during treatment quietude is important. Rheumatic cases do not do well in the rush and bustle of ordinary life, and any tendency to introduce this into resorts which claim to treat patients suffering from rheumatism is certainly to be deprecated.

Dr. SYDNEY D. MITCHELL: Chronic rheumatic joint disease, with its wide social and economic implications, apart from purely medical considerations, must—like pulmonary tuberculosis—necessarily have important psychological aspects.

A study of these was made at the St. John Clinic and Institute of Physical Medicine from 1932 to 1934 by Dr. Philip Ellman and myself and published in the Royal College of Physicians' "Reports on Chronic Rheumatic Diseases" [1].

Forty cases of the rheumatoid type of arthritis, and 40 cases of the osteo-arthritic type, corresponding to the classification described by one of the authors [2], were selected for examination. All were typical of their groups, mixed cases being excluded; otherwise they were taken quite at random from the Out-patient Department.

The psychiatric examination which I undertook consisted of (*a*) an investigation of the personality, i.e. the behaviour of the individual as a whole from early childhood up to the onset of the illness. (*b*) an investigation of the personality following the onset.

In the investigation of personality, although facts and tests by accurate measurement are ill-defined, the psychologist, like the layman, tends to classify people into types. Classification inevitably implies abstraction. The only accurate conception is of a continuous scale with most persons falling in the middle but tending towards one or other extreme end.

With these provisos we adapted Bleuler and Kretschmer's postulation of two components, syntonic and schizoid, in each healthy personality.

In the *syntonic type* the whole personality freely expresses a definite emotion suitable to the situation. The train of thought is disturbed only by overvaluation of what conforms to it and undervaluation of what disturbs it. The mood remains at an average pace and relatively uniform throughout life. If, however, the mood fluctuates, we speak of cyclothymic personalities or, in marked cases, of manic-depressives. Again the mood may permanently deviate to depressive or manic states.

The *schizoid type*, on the other hand, shows a lack of uniformity of emotional expression and co-existence of different strivings. Schizoid sub-groups include: (*a*) Those who indulge in free phantasy thinking in contradistinction to reality. (*b*) The paranoid type who sees in the actions of others an undue reference to himself. Extreme degrees of the schizoid type are called schizophrenic. The neuroses also manifest themselves essentially on a schizoid basis, e.g. the interference of one impulse with another, the lack of adjustment to situations, as in the common anxiety state. In hysteria, however, one also recognizes in the emotional lability a syntonic component.

In the 40 *rheumatoid arthritics*, schizoid features, especially morbid anxiety, predominated in 27 cases before the onset of the illness and in 25 following the onset. Syntonic and related features predominated in only 10 cases before the onset and in 9 following it.

In the 40 *osteo-arthritics*, on the other hand, syntonic and related features, especially depression, predominated in 22 cases before the onset and in 19 following it. Schizoid features predominated in 14 before, and in the same number following, the onset.

Attention was also paid to any history of special worry over exogenous factors immediately prior to the onset of the illness. This was obtained in 15 rheumatoid and 5 osteo-arthritics. The features varied from illnesses and accidents to relatives and unusual pressure of work or difficulties at work to matrimonial disharmony.

A study was also made of external causes of worry following the onset of the illness. One naturally found that the crippling effects of arthritis led indirectly to interference with earning capacity and consequent financial difficulties. There was also, of course, in many

cases, inability to indulge to the same extent as before in habitual pleasures. In addition, other physical disabilities, such as the menopause and arterial hypertension, played their part in a number of osteo-arthritics. Apart from these factors, however, there were histories of independent external worries in 23 rheumatoid and 5 osteo-arthritics. These ranged from family illnesses and matrimonial disagreements to financial difficulties unrelated to the direct results of the arthritis.

One must, of course, allow for the fact that any patient suffering from a psychopathic state will tend to seek querulously in external misfortunes a justification of his morbid mental state or his physical disability. Nevertheless, the presence of such continuing external factors is of importance for prognosis.

The study of controls was also considered. Three methods of approach suggested themselves: (*a*) A series of cases suffering from a variety of chronic physical illnesses other than chronic arthritis, (*b*) a series of cases suffering from one type of chronic illness, (*c*) a series of so-called healthy persons. (Incidentally a scientific standard of mental and physical health is no easy matter to assess.) After careful consideration it was finally decided that an over-simplification of the mental and physical factors concerned would be inevitable and there the matter was abandoned.

In reviewing our results we particularly noticed the prominence of morbid anxiety in the rheumatoid arthritics. In the osteo-arthritics there was a slight excess of syntonic and related features, but the high percentage of morbidly anxious persons cannot be ignored. Our genetic studies reinforce the general psychiatric view that the make-up of the previous personality is the main factor in the type of mental state following physical illness.

Allusion has already been made to the fact that arthritis may be only one of several misfortunes which beset the patient at about the same time. One is, therefore, not justified in speaking of a *direct* mental reaction to the physical illness without very full investigation of each case.

Does mental disturbance lead directly to organic disease in the arthritic? In the present state of knowledge we feel that judgment should be suspended. It seems likely, however, that, in the arthritic, both mental disturbance and organic disease are evidence of a general biological inadequacy.

I will conclude with a short reference to the important subject of treatment of the mental aspects of arthritis. For the average patient the mere opportunity of unburdening himself of his difficulties to a sympathetic listener will be helpful. Apart from this, suggestion and persuasion are all that will be possible for most. Certain selected cases might, however, with benefit be referred to a psychiatrist for more intensive psychotherapy. The danger of suicide should always be borne in mind, especially in depressed cases. It was evident in a large number of our series. The use of sedatives and hypnotics, as indicated, and indirect psychological treatment such as occupational therapy and the attempted removal of irritating exogenous factors, are valuable additional aids. Trained social workers attached to institutions could do much in this direction.

We feel also that the establishment of more and better staffed residential institutions for chronic diseases, including arthritis, is an urgent necessity. The Rheumatism Unit at St. Stephen's Hospital is an excellent step on the part of the London County Council in this direction. Sanatoria might well be planned on similar lines to those existing for tuberculous patients, where there is, or should be, ample catering for their physical and psychological requirements, that is for viewing the individual patient as a whole.

References.—1 ELLMAN, P., and MITCHELL, S. D. (1936), R.C.P. Reports on Chronic Rheumatic Diseases, No. 2. 2 ELLMAN, P. (1936), *Post-Grad. Med. J.*, **12**, 211.

Dr. KERR PRINGLE said that apprehension with regard to the future in relation to finance, occupation and progress of the ailment was an important factor in delaying and preventing recovery in cases of chronic rheumatic disease, quite apart from the ætiological factor, such as infection, endocrine imbalance, shock, &c.

In this respect Great Britain was behind America and Sweden, where the importance of distracting the patients' attention from their disabilities by some form of occupational therapy was recognized. One had only to go round the hospitals here, devoted to the treatment of these conditions to see how the patients, when not having treatment, were sitting about, doing nothing but talking about their ailments, when their time might have been much better employed by learning to do something useful so far as their disability permitted. By this means their attention would be drawn away from their ailments and they would gain fresh hope for the future.

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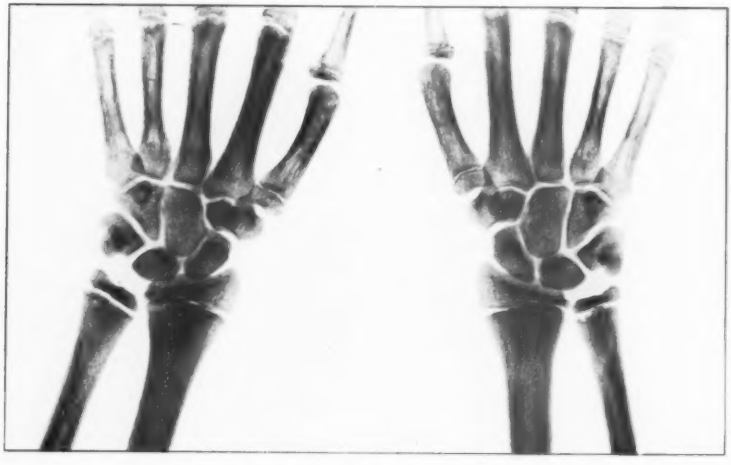
PLATE I

Pelvis showing minor degree of coxa vara with changes in the metaphyses due to renal rickets.



The metacarpals and one ulna show signs of renal rickets.

V. H. ELLIS : Adolescent Coxa Vara due to Renal Rickets.

UNIV. OF MICH.

Section of Orthopædics

President—A. Rocyn Jones, F.R.C.S.

[*October 5, 1937, contd.*]

Adolescent Coxa Vara due to Renal Rickets.—V. H. Ellis, F.R.C.S.

J. R., a girl aged 15 years, had been noticed to limp for six months. The right hip appeared to be chiefly affected. No history of injury, nephritis, or other severe illnesses.

The patient was below the average height for her age, but otherwise of normal development. There was a moderate degree of knock-knee. The legs were of equal length. There was slight fixed external rotation of the hips and internal rotation was limited on both sides. Beading of the ribs could be felt.

A skiagram of the pelvis shows a minor degree of slipping of both upper femoral epiphyses. The metaphyses, both of the heads and of the great trochanters, show widening and rarefaction. A skiagram of the hands shows stippling of the metacarpals, said to be typical of Type A renal rickets, and there are also rickety changes at the distal end of the shafts of the 2nd, 3rd, and 4th metacarpals, and of the ulna on one side. (See Plate I.)

Blood urea 160 mgm. %; albuminuria 0·1%; blood calcium 10·7%.

The following were also shown :—

Post-Traumatic Chronic Inflammation of the Calf.—G. R. Girdlestone, F.R.C.S.

(1) Congenital Coxa Vara. (2) ? Osteochondritis Acetabuli. (3) Sarcoma following Fracture of the Clavicle.—Norman Capener, F.R.C.S.

Specimen from a Case of Pott's Paraplegia.—H. J. Seddon, F.R.C.S.

(1) Arthrogram of the Hip-Joint. (2) Osteochondritis of the Base of the 3rd Metatarsal. (3) Calvé's Osteochondritis of the Spine.—J. A. Cholmeley, F.R.C.S.

[*November* 2, 1937]

Pellegrini-Stieda Lesion.—W. D. COLTART, F.R.C.S.

R. S., male, aged 40. Seen in Orthopædic Department, St. Bartholomew's Hospital, April 1937.

History.—On November 21, 1936, he was injured while working on board ship. He received a blow on the head, and became unconscious. The left sterno-clavicular joint was dislocated, and the right knee was injured; he cannot remember the method of trauma to the knee. The knee had been painful since the accident, both on activity and when at rest.

Six months' physical treatment, consisting of massage and passive movements, had produced no relief.

On examination of the right knee no fluid was found in the joint, but there was thickening over the internal condyle of the femur and inner side of the joint. The whole of this area was tender. No definite bony swelling could be felt. Extension of the knee was limited to 170°, and flexion to 90°. A skiagram taken at this time (Plate II, fig. 1) shows the typical appearance of the Pellegrini-Stieda lesion.

Treatment.—The knee was first immobilized in a plaster-of-Paris back splint, and the patient was kept at rest for six weeks; at the end of this time the pain was completely relieved, and the patient was able to walk without pain, wearing the splint. He was then given a course of faradism to the quadriceps muscle, and was told to give up the splint gradually. The condition of the knee improved for about eight weeks only, but was then arrested, and no further improvement was noted during a further period of four weeks. At this time he still had pain in the knee after walking more than half a mile. On examination extension was found to be full, but flexion was still limited to 90°, with pain over the inner side of the joint, on attempting further movement. A skiagram (fig. 2) taken at this time (September 1937) showed condensation of the area of ossification. The patient was admitted to hospital, and on September 2, 1937, an operation on the knee was performed, and the bony fragment was excised. The abnormal bone was situated over the internal condyle of the femur, was completely covered with fibrous tissue, and was apparently continuous with the internal condyle. There was a flake-like superior projection which passed above the condyle anterior to the adductor magnus tendon; the bony fragment was not connected to this tendon. After dissection it was possible to pass a gouge deep to the bony fragment and separate it from a fibrous bed on the internal condyle. The upper end was freed easily, but the lower end was attached to a superficial layer of the internal lateral ligament of the knee-joint, from which structure it had to be dissected. After removal of this piece of bone the medial capsule of the knee-joint was still intact, and the joint was not unstable on lateral movements. The leg was immobilized on a splint for two weeks after operation; this was followed by physical treatment to the knee.

Improvement has been maintained, and to-day the patient has no pain in the knee, and can walk well. Extension is full; flexion is still limited to 90°. The quadriceps muscle is not yet up to full strength; there is no lateral instability of the joint. A skiagram (fig. 3) taken at this time shows some re-formation of bone.

Figures 4 and 5 show the piece of bone after removal. It is 5 cm. long and 2 cm. in width at its broadest part. A microscopic section shows bone with well-formed Haversian systems; the marrow spaces contain hæmopoietic tissue.

Comment.—It is worthy of note that the symptoms showed no improvement with active physical treatment, but immediately improved following a period of rest. Indications for operation were the cessation of improvement, and the X-ray

PLATE II

FIG. 1.—April, 1937.

FIG. 2.—September, 1937.

FIG. 3.—November, 1937.

FIG. 4.

FIG. 5.

Fragment of bone after removal. Actual size. (Fig. 4, Lateral view, Fig. 5, Anterior view.)

W. D. COLTART : Pellegrini-Stieda Lesion.

PLATE III

P. W., before operation, March, 1936.

P. W., after operation, April, 1937.

D. McCRAE AITKEN: Tuberculosis of the Patella.

appearances, showing condensation of the bony fragment. At operation, the bony fragment was quite definitely attached to the internal lateral ligament of the knee, but was clearly separate from the internal condyle of the femur, and from the tendon of the adductor magnus. The histological appearance of the fragment was that of true bone, containing hæmopoietic marrow, and not simply of a calcified matrix. Although skiagrams taken recently show that re-formation of bone has taken place the patient's symptoms are now completely relieved.

I am indebted to Mr. S. L. Higgs for permitting me to treat this case.

POSTSCRIPT (November 15, 1937) : The movement of flexion in the knee is now almost full.

Tuberculosis of the Patella.—D. MCCRAE AITKEN, F.R.C.S.

In May 1933 I reported to this Society two cases of tuberculosis confined to the patella.[1] In both cases an operation was performed removing part of the outer hard bone, and in one case scooping out the soft area. In the other case the soft area contained caseous matter and necrosis. Both cases made good recovery, with regeneration of the bone structure of the patella and with good movements of the knee. The case shown to-day (*see* Plate III) is similar, in a boy first seen in 1935, with a history of swelling of the knee extending over about two years. On admission the knee was markedly swollen and clinically tuberculous. Skiagrams showed several spots of rarefaction in the patella, with no involvement of the other bones. The softened areas were scraped out : no tubercle bacilli were found. The immediate result was relief of pain and swelling. When the patient was allowed to walk the swelling reappeared, although the structure of the patella was well restored. In 1937 there was a cavity in the patella which seemed to contain some caseous or calcareous matter, and the patella was removed in February of that year. As the patella was being removed, the anterior surface gave way and a small quantity of very thick caseous matter exuded. After a few weeks movements of the knee in bed were begun, and the boy has now been walking freely for three months. He can extend his knee almost fully and can flex to 30° (*see* Plate III).

Plastic Operation for Congenital Absence of Thumb.—C. LAMBRINUDI, F.R.C.S.

E. K. E. This patient consulted me in January 1937 and asked if his hand could be made more useful. There was congenital absence of the radius and the thumb, but the carpus had been successfully arthrodesed with the ulna eighteen months previously. His chief complaint was inability to grasp things, owing to stiffness of the fingers and absence of the thumb.

Condition on examination (figs. 1 and 2).—The whole of the inner segment of the hand, including the 5th finger, was quite normal and powerful. The other three fingers were atrophied and there was very little movement in the metacarpal or phalangeal joints. This appeared to be due to stiffness of the capsule and contracture of the flexor and extensor muscles of the fingers. The interosseous muscles of the index finger were, however, particularly well developed. The patient was extremely sensitive about the appearance of the hand, always kept it in his pocket, and used it as little as possible. I suggested to him the possibility of converting the index finger into a thumb and told him to overcome his sensitiveness, to use his hand as much as possible, and to report four months later. When I saw him in June he was able to use the

[1] *Proceedings*, 1933, **26**, 1338. (Sect. Orthop., 72).

P. W., after operation, April, 1937.

P. W., before operation, March, 1933.

D. McCRAE AITKEN : *Tuberculosis of the Patella.*

atrophied fingers a little better, and I was again struck by the exceptional development of the intrinsic muscles of the index finger ; I therefore decided to operate.

Operation (23.6.37).—An incision was made along the dorsum of the first cleft, forking at the level of the metacarpophalangeal joint. From there the two incisions were carried on to the palmar aspect, for about an inch. A flap was dissected up, and so to speak, unfolded at the free margin of the web, thus converting the whole web into a long flap. The interosseus ligament was then divided and the 2nd and 3rd metacarpal bones separated. The head of the 2nd metacarpal bone was drilled and a Brock's pin inserted. An oblique osteotomy of the metacarpal was then made and the distal fragment carrying the phalanges was rotated through an angle of almost 80°. The wound was sewn up and two raw areas were covered by a Thiersch graft. The forearm and hand were put in plaster with the new thumb fixed in proper position by incorporating the Brock's pin in the plaster.

FIG. 1.—Before operation. Note atrophy of the three outer fingers, and well-developed intrinsic muscles of the index finger.

FIG. 2.—Before operation. Dorsal aspect.

FIG. 3.—After operation. Dorsal aspect.

Present condition.—The patient can oppose his new thumb and middle finger (fig. 3) and can grasp both large and small objects (figs. 4, 5 and 6). He asserts that his hand is more useful. But one unfortunate thing has happened—the extensor tendon controlling the new thumb has ruptured. At the operation I noticed that when rotating the distal fragment the extensor tendon was very much stretched and riding over the sharp margin of the divided bone. I am shortly going to repair this tendon.

FIG. 4.—After operation. Showing the action of the intrinsic muscles of the new thumb.

FIG. 5.—Showing lines of incisions and flap.

FIG. 6.—Patient is beginning to write quite well.

Mr. Lambrinudi's Case of Plastic Operation for Congenital Absence of Thumb.

The following cases were also shown :—

Pathological Fracture of Humerus.—F. F. RUNDLE, F.R.C.S.

Unusual Fracture of Neck of Radius in a Child.—E. P. BROCKMAN, M.Ch.

Unusual Rarefaction following Fracture in a Case of Fragilitas Ossium.—H. J. BURROWS, C.B.E., F.R.C.S.

Fibrocystic Disease of Upper End of Femur.—C. LAMBRINUDI, F.R.C.S.

The following demonstrations were given :—

The Peg-leg Walking Plaster for Congenital Dislocation of the Hip (Cinematograph film).—NORMAN CAPENER, F.R.C.S.

Special Apparatus and Splints.—MAUD F. FORRESTER-BROWN, M.S.

Section of Epidemiology and State Medicine

President—Sir ARTHUR MACNALTY, K.C.B., M.D., F.R.C.P.

[*November* 26, 1937]

The Contribution of Industry to Medicine

By H. H. BASHFORD, M.D., M.R.C.P.Lond.

(*Chief Medical Officer to the Post Office*)

PERHAPS I should say at once that this title was chosen because I believe that Industry, given certain conditions, is capable of making a great and indeed essential contribution to Medicine. But I would prefer to return to this point later, and meanwhile I would ask you to forgive me for the personal arrogance that the title has perhaps suggested. Although, during the last few years, I have kindly been given the opportunity of seeing a certain amount of the inside life of various large industries, particularly in respect of their welfare arrangements, my own experience, for the last thirty-odd years, has been chiefly confined to the Post Office.

But, as you no doubt realize, the Post Office, though a branch of the Civil Service, is in fact, numerically speaking, the largest industry in these islands and also probably the most various. Its 260,000 employees, men and women and boys and girls, include such large and differently employed groups as postmen, sorters, telegraphists, engineers, skilled workmen, motor-transport drivers, wireless operators, telephonists, and of course very considerable bodies of men and women employed on administrative, clerical, and accounting duties. But it has certain features in which at present it differs from many other large industries. Thus, for the great majority of its people, it is a life-long pensionable service, with privileges as regards sick pay and holidays that are not always to be found elsewhere. It inclines, therefore, particularly on the men's side, to be a somewhat more stable industrial body than many ; and its service has been prefaced by a thorough medical examination at entrance—and usually by two such examinations.

Further, it is one of the conditions of employment that every established pensionable Post Office servant, under a salary of, roughly, five pounds a week, receives free medical attention of a good general medical practitioner range, and this automatically implies an extent and intimacy of medical care and observation that does not exist in many other industries.

Allowing, however, for these differences, there must necessarily, I think, be in the Post Office many human problems and experiences that are common to all industrial activities in which men and women and boys and girls are employed in large numbers. The Post Office is unique in that there is in this country no other body of industrial workers of anything approaching its size—more than a quarter of a million people—that has accurate sick records of all those people from the ages of 16 to 60 and often from 14 to 60—sick records that are analysed yearly in terms of occupational groups and of geographical groups, and in respect of workers in typical industrial cities, inland non-industrial towns, and seaside places.

These records extend back for a great many years—as an industrial medical service, that of the Post Office dates from the middle of the last century—and you will readily appreciate how such records lend themselves to certain, and I think, very valuable, types of research. They make it possible, for instance, to assess the significance—or non-significance—of various medical or surgical conditions in terms of everyday, actual working experience as no follow-up department, however carefully conducted, of any hospital or individual physician or surgeon could possibly do. And the same is true of various forms of medical or surgical treatment.

There are still, I am sure, untapped mines of information contained in these tens of thousands of life-histories. But perhaps you will forgive me for referring to some of the work that we have been able to do in this way, and I must again ask your

forgiveness because some of this has already been published and may perhaps be familiar to you.

Pulmonary Tuberculosis. Peptic Ulceration. After-histories

First, I should like to refer to the condition of pulmonary tuberculosis, as we in the Post Office have experienced it. Taken as a whole, the incidence of this compares very favourably with that in the community at large, and during the last twenty years this incidence has shown a steadily downward trend. But we necessarily encounter a good many of these cases, and recently we were able to publish an analysis of 3,755 cases observed over the last twenty years, cases of which we know the exact incidence and everything that has happened to them afterwards. Briefly we have found—although, as long as there remains a reasonable prospect of recovery to render regular and efficient service in the future, the Post Office is willing to allow very prolonged periods of sick absence—that quite constantly only 50% of all new cases are able to return to work at all. Of this 50% that return to us, cured or arrested, there is a constant wastage of another 48% during the following ten years, due to recurrent pulmonary tuberculosis or other forms of ill-health. For those remaining at the end of ten years, the prospects are somewhat better, and the wastage, during the next five years, has not been more than 14%.

Another analysis that we were recently able to publish was that of the after-histories of a group of 430 cases of gastric and duodenal ulcer, confirmed by X-ray investigation, and returned to work after various forms of surgical and medical remedial treatment. Briefly, again, we have found, after observations extending from not less than three and up to twenty years, that 31% of all these cases, however they may have been treated, regularly incur a month's sick absence or more every year for recurrent digestive disorders or other forms of ill-health, and another 27% of them sick absence for from two to four weeks every year. I doubt if it would have been possible anywhere else to have obtained, in either of these instances, quite so accurate a long-distance picture of the effect of these diseases on everyday working capacity—possibly, in each case, somewhat more sombre than that of the clinician and the medical textbooks.

Adolescent Albuminuria: Post Office Experience

On the other hand, there have been abnormalities of which we have been able to take a brighter view than that current, or at one time current, in Medicine as a whole. Thirty years ago, when I first joined the medical staff of the Post Office, no boy presenting the condition of albuminuria, however healthy-seeming he might otherwise be, was acceptable for any pensionable service, and he was usually uninsurable, or only insurable at a heavily loaded premium. If the condition was discovered by the average family, or school, doctor, he was usually forbidden to play such games as "rugger" or "soccer", or to row; and in fact all these boys were under suspicion, if no more, of being in the early stages of chronic interstitial nephritis and consequently either doomed or damaged lives.

A few of you, who are old enough, may remember, as I do, certain forlorn medical students in whom this condition had been accidentally discovered.

Owing to the relatively large numbers of these boys, however, that were regularly presenting themselves for employment in the Post Office, one of my predecessors, perhaps rather in advance of the general medical opinion of his time, had decided to take a chance and advise the acceptance of some of them. Accordingly I was able, some thirty years ago, to find a group of 30 such cases and to re-examine them—and their sick records—after periods of service varying from seven to fourteen years. Twenty per cent. of them still exhibited the condition, but all were in apparently good health and their sick records were normal. With the exception of three who had left the Service for quite extraneous causes, two who could not be traced, and one who had died seven years later from acute nephritis, I was able to examine the whole group again seventeen years later, the youngest being then 43 and the oldest 54, and

without exception they were all in good health. None of them presented any signs of renal disorder, and eighteen of them had sick records well below the average of the whole service.

Later I found that, in a consecutive series of 1,000 14-year-old boys, one in every 20 presented the condition, and these included boys of every size and shape and temperament, the weed and the athlete. Further, in 1932, Dr. G. W. Theobald, examining our material, found that in a group of 5,000 girls about 16% presented the condition, and more recently I was able to review a consecutive series of 100 of these, after a period of fifteen years' observation. In no case had there been any evidence of subsequent renal impairment, and the average annual sick-rate of the group was approximately the same as that of the whole service during the years in question.

All these observations have, from time to time, been published, and I think they have helped to demonstrate, as probably few others could have done with equal accuracy, that this condition is *per se*, of no material importance whatever—a view that has now, I think, filtered very generally through both the medical and insurance and service worlds, thus lifting a burden of quite unnecessary anxiety from a very large number of young shoulders.

Comparative Physique of Young Entrants

Another instance of the rather unexpected value of such records as have been kept in the Medical Branch of the Post Office was in respect of the physique of the present generation of young Londoners as compared with the last. A few years ago, thanks to our figures, we were able to compare a quite haphazard, consecutive, unselected series of 400 boys and girls of 16—candidates applying for Post Office employment and coming from the same sorts of London families and neighbourhoods as they have always done. We found—and these figures may also be familiar to you, as they have been published and referred to rather frequently—that the boys of to-day averaged 16 lb. more in weight and 1½ in. more in height than those of twenty-five years ago, and that the girls averaged 9 lb. more in weight and 1 in. more in height than the girls of twenty-five years ago. As far as I have been able to discover, these were the only available actual comparative figures in this particular field of observation.

Those are a few instances of what has been obtained—and an indication, perhaps, of what might be obtained—in respect of the assessment of particular medical and physical conditions in one large industrial concern with accurately kept data. I might perhaps refer to one or two examples of the help that is thus also possible in the way of assessing the long-distance, practical, workaday value of particular forms of treatment, psychological investigations, and methods of hygienic or public health control. I will give one example of each.

Anti-catarrhal Vaccine: A Three-years' Experiment

Four or five years ago it was suggested to the Post Office that it might be a valuable measure to provide routine inoculation of anticatarrhal vaccine for the whole staff as a method of preventing or reducing the considerable amount of sick absence due to colds and other catarrhal conditions. A preliminary experiment was in consequence decided upon, and volunteers were asked for from several selected large cities in various parts of the kingdom and from one large headquarters department. For the purposes of the experiment it was decided to include amongst catarrhal complaints all illnesses certified as being due to the common cold, nasal and bronchial catarrh, influenza, simple pyrexia, febricula, chill, bronchitis, and coryza. The vaccine used consisted of *Bacillus influenzæ*, *Staphylococcus pyogenes* (*aureus* and *albus*), *Streptococcus pyogenes* (hæmolytic and non-hæmolytic), Pneumococcus Types I and II, *B. coryzæ segmentosus*, and *B. friedländer*.

The first series of inoculations took place in the autumn of 1933, the total number of volunteers being 883. The second series was in the autumn of 1934, when 536 of the original volunteers again presented themselves. In the third series in the autumn of 1935, 374 of the 536 offered themselves once more. During this period there was

no major epidemic of influenza, and the three years could be regarded as normal in respect of the general incidence of catarrhal complaints. In the first year there were control groups amounting to 3,895 non-inoculated Post Office workers ; in the second year there were control groups amounting to 4,096 non-inoculated Post Office workers, and in the third year there were control groups amounting to 4,499 non-inoculated Post Office workers.

To summarize the results : It was found that, at the end of the first year's experiment, the average sick absence for catarrhal disorders amongst the volunteers was less by half of one day than that of the non-inoculated controls. At the end of the second year the average sick absence for catarrhal disorders amongst the volunteers was 0·1 day higher than in that of the non-inoculated controls. At the end of the third year it was 0·2 day higher than that of the controls. For the combined period the average sick absence for catarrhal disorders of the inoculated volunteers was only 0·1 day less than that of the non-inoculated controls.

A comparison was then made—omitting the winter of 1932–33, when there had been a very widespread and relatively severe epidemic of influenza—between the sick absence for catarrhal disorders of the 374 volunteers, who had thought it worth while to persist throughout the experiment, with their previous sick absence for these disorders between 1930 and 1932. The average reduction observed during the three years of the experiment amounted only to 0·4 day.

A comparison was then made in respect of the 33 volunteers, whose average annual sick absence for catarrhal disorders before inoculation had amounted to ten days or more, and in fact this group, as a whole, had averaged 21·9 days for catarrhal disorders. During the period of the inoculations this was reduced to 10·9 days. But, against this, there was a group of 17, whose average annual sick absence for catarrhal disorders had only amounted to 3·8 days before inoculation and had increased to twenty days during the period of inoculations.

I do not wish to claim any exaggerated scientific value for this series of observations or to base any generalizations upon it. But it was sufficient, I think, to answer the particular question that had been posed to us and to indicate that the routine provision of anti-catarrhal vaccine for the staff, as a whole, was not yet a measure that could be justified by the results experienced.

Vocational Guidance

The second example refers to an interesting series of observations made, about twelve years ago, by two well-known psychologists on behalf of the Industrial Fatigue Research Board (since merged in the Industrial Health Research Board). The subjects were 55 boys and 60 girls, all adolescent and at the beginning of their careers in the Post Office, and the object of the investigation was an assessment of their liability to develop inefficiency at their work as the result of nervous disorders or an inadequate psychological " make-up ". They were all submitted by one of the observers to various mechanical reaction and co-ordination tests, and each of them was interviewed by the other with a view to discovering obvious or latent psychological abnormalities.

Recently it became possible to review this group at the end of ten years, when their sick records were examined, and an independent contemporary report on their characters and efficiency from their present supervising officers was obtained in the case of all those still in Post Office employment. The results were as follows : Of the 17 boys placed in a " serious symptom " psychological group, 16 were still in the service, one having been transferred to another department. None of them had incurred an abnormal sick record and, in every case, at the end of ten years, the character-and-efficiency report was excellent. Of the 16 boys placed in a " slight symptom " psychological group, one had resigned, three had been transferred to other departments, and two were not traced. Of the remaining 11, one had a definitely poor character-and-efficiency report, one a slightly qualified report, the remaining nine reports being excellent. None of the 11 had abnormal sick records. Of the 22 boys placed in a " no symptom " psychological group, 14 were still in the service, seven

having been transferred to other departments, and one having been dismissed. Of the remaining 14, nine had excellent reports, three slightly qualified reports, and two definitely qualified reports.

It will thus be seen, on the basis of ten years' observation, that in the case of the boys the original psychological groupings had scarcely been reflected in practical working experience.

Turning to the girls: It must be remembered that, as in other industries, these form in the Post Office a far less stable population, and there are many resignations, in the earlier years of service, for marriage and other reasons. Of the eight girls placed in a "serious symptom" psychological group, only four were left at the end of ten years, one having been retired on medical grounds and three having resigned. Of the remaining four, two had excellent character-and-efficiency reports, one a definitely, and one a slightly, qualified report. The sick records of the four were rather high. Of the 15 placed in a "slight symptom" psychological group, 10 remained in the service, five having resigned. Eight had excellent reports, and two definitely qualified reports. Three had rather heavy sick records, those of the remainder being normal. Of the 37 placed in a "no symptom" psychological group, the appointment of one had been subsequently cancelled, 22 had resigned, and 14 remained in the service, but 18 reports were available. Of these 12 were excellent, five were slightly qualified, and one was definitely poor. Fifteen of the sick records were less than the average.

It could thus perhaps be argued that, in the case of the girls, there was a somewhat nearer approximation between the results of practical working experience and the original psychological groupings, but, so far as it goes, the evidence can hardly be called very convincing. And it would appear, though it would obviously be unfair to dogmatize too strongly on so small a series, that the general practical value of this particular form of vocational guidance has yet to be established.

Quarantine and Contacts

Thirdly I would mention, as perhaps being of particular interest to this Section of the Royal Society of Medicine, the experience of the Post Office, as the largest industrial concern in the country, in respect of quarantine and the treatment of contacts with infectious diseases. This has naturally been a subject of special concern to the Post Office, both from the point of view of the protection of the public with which it deals, and that of its own employees, and also from the economic aspect. For enforced absence, due to contact with infectious disease, is financially equivalent to sick absence, and represents equally a cost or loss due to illness, and I might perhaps say here that, in so vast a concern as the Post Office, each day of the annual general sick rate for the whole staff of its workers represents a yearly financial cost or loss to the Department—and, since the Post Office is not a privately owned concern, ultimately to the country—of a very considerable sum.

From all these points of view, therefore, the problem of the contact is an important one, and many years ago thousands of working days were regularly lost by contacts, otherwise healthy, remaining for various periods upon enforced absence, owing to the incidence in their homes or lodgings of cases of scarlet fever, measles, diphtheria, chicken-pox, and the like. But, as you know, there has been a considerable change, during the last two generations, in our general conception of the nature of the causal agents of these zymotic diseases and the methods by which infection is spread. For many years past the policy of the Post Office has tended in the direction of abolishing quarantine and permitting contacts—provided that the relative invalids have been suitably isolated or removed to hospital—to remain at work, if in good personal health and under appropriate medical supervision.

This has meant a good deal of medical educative work, since there has been, and still to a certain extent exists, not only in the lay mind but also in some medical minds, a belief that contacts are *per se* sources of potential danger. For this reason, and although all contacts are dealt with locally according to routine regulations, varying a little with various diseases and circumstances, it has been found administratively

advisable for every such contact to be notified at once to our Headquarters Medical Branch, so that the procedure in each case can be observed and approved and exceptions advised upon on the day of receipt.

This would not be the occasion upon which to enter into the details of our particular procedure. But, speaking generally, this policy, now established for many years, has saved thousands of days of what we have come to regard as quite unnecessary enforced absence, and there has been no evidence whatsoever of any increased incidence amongst the Post Office staff of these zymotic fevers, or of any local epidemic arising in any office or department in consequence, or indeed of any of his or her fellow-workers having been infected by a contact.

For some years, too, we have taken steps for any contact, subsequently acquiring the relative disease, to be notified to us, and the results of this, for the last ten years, may perhaps be of some interest. Thus we have found that in 17,844 contacts with scarlet fever, only one in every 251 has subsequently acquired the disease. Of 17,436 contacts with measles only one in every 670 has subsequently acquired the disease. Of 7,697 contacts with diphtheria only one in every 274 has subsequently acquired the disease. Of 7,000 contacts with chicken-pox only one in every 218 has acquired the disease. And of 3,463 contacts with mumps only one in 101 has subsequently acquired the disease.

Sick Absence. General Causes. The Age Factor

Finally, perhaps a word or two might be said about the chief causes of sickness and disability for work in the experience of the Post Office as an industry. This must admittedly be a rather rough and ready classification, depending very largely, as it does, on the face value of medical certificates. But, allowing for this, it may be said, very generally on the basis of our present information, that about 30% of all our sickness is included in the catarrhal and respiratory group of disorders, and this is true both of men and women. About 10% is included in the digestive disorder group, and again this is true both of men and women. On the men's side about 10% is incurred in the rheumatic group of disorders, and about 4% on the women's side. About 6% is incurred on the men's side in the nervous group of disorders, and about 14% on the women's side.

Turning to the average amount of sickness incurred in age-groups, a recent analysis by the Government Actuary of the whole of the sickness incurred in the Post Office, excluding the engineering side, over three triennia since the War, has shown that men between 40 and 60 incur 55% more sickness, as a group, than men, as a group, under 40 ; and women over 40 incur, as a group, about 58% more sick absence than women under 40. The older people do not incur so many separate sick absences, but those that do occur tend to be of longer duration.

The age-composition of any industry or community is therefore clearly a factor of considerable importance in assessing the real significance of the sick absence that it incurs, and is of equal importance in comparing the sick-rates of one industry with another, or of one community with another, or with itself at some other period. There has, for example, in the Post Office, been a very remarkable alteration in its average age-composition, even in the last twelve years. Thus in 1923 48% of its men were 40 years of age or over and 18% of its men were 50 years of age or over. In 1935 56% of its men were 40 years of age or over and 25% or a quarter of all its men, excluding the engineering side, were 50 years of age or over ; and there has been a similar increase in the average age-composition of its women employees. In 1923 only 13% of these were over 40 whereas, at the beginning of 1935, 22·9% were over 40.

Measures such as improved environment, more careful attention to personal—and perhaps especially to dental—health, and various preventive measures, can of course go far to counteract the effect upon sick-rates of this increasing proportion of middle-aged and elderly people. But, other things being equal, it would seem that the averagely older industry or community must probably expect a higher sick-rate than the averagely younger industry or community.

And, as a last word, there is that vague class of illness in which there would seem to be a factor, not of true malingering—which personally I have found to be exceedingly rare—but of youthful irresponsibility, of what might be vulgarly termed gutlessness, or of some condition of self-pity or maladjustment of general perspective. A considerable amount of this type of sick absence is, I am sure, due to atmosphere, in the psychological sense of the word, and the atmosphere, in this sense, of an office or department is, I am equally sure, largely dependent upon the particular man or woman in charge of it. A fretful or unsympathetic supervisor or controller, however technically competent, or a supervisor or controller, who is himself of the introspective, self-regarding type, can create an infection which permeates right through his particular charge, just as a healthy, kindly, competent, and understanding head of a department can radiate an influence of precisely the opposite sort.

Allowing for this, however, in any large working community, there will be a few men and women whose individual sick absences fall into this rather vague category, and they require very careful and patient medical observation and treatment. A quiet talk may in some cases suffice to alter the whole complexion of such a sick record, or again attention to some such source of trouble as neglected teeth or septic tonsils may have a similar effect. But if all such measures fail, then I think the only practical method is to accept these sick records at their face value and either advise retirement or let it be known that this is under consideration. In some cases this latter course, bringing the people concerned face to face with a perhaps serious reality, may itself have a tonic—and, medically speaking, beneficial—effect. For example I have notes of a consecutive series of 40 such cases of repeated, relatively trivial, accumulating sick absences, in which there was apparently an underlying factor of the kind I have described. Over a period of about four years, these 40 people had, among them, incurred 736 sick absences, totalling 6,194 days. Following kindly advice that, if these sick records persisted their retirement on grounds of persistent ill-health would probably have to be considered, during the next six months the whole 40 people merely incurred fifty-four days' sick absence among them. In other words their six-monthly average of illness dropped abruptly from nineteen days a head to 1·3 days a head.

It is true, of course, that many large industries do not at present keep accurate sick records, or records of their retirements due to ill-health and the average age of such retirements, without which mere sick records are largely valueless. But other large industries are now beginning to do these things, and indeed it is difficult to see how any industry can otherwise really assess the health and efficiency of its all-important human material and the effects upon this of changing environment or alterations of technical processes. Even for their own industrial success and efficiency it would surely appear to be essential that such records should be kept, though this is not the point I wish to emphasize at the moment.

But given any large self-contained industry, with such records carefully kept over a number of years, it seems to me that you have, as it were, a sort of natural laboratory, where a kind of unselfconscious research is always going on for those who have eyes to see it and the patience to record it. It is there that you can test, as in no other way, the practical issues of Medicine, and bring to the bar of everyday, working experience the claims of the surgeon and physician and the teaching of the textbooks. It is surely not impossible that there are some such contributions still waiting to be made by Industry which, in some respect or another, and in some particular field, may alter the whole outlook of Medicine.

REFERENCES

BASHFORD, H. H., and SCOTT, W. L. (1936), *Lancet* (ii), 1115.
Id. (1935), *ib.* (ii), 710.
BASHFORD, H. H. (1926), *Lancet* (ii), 1305; (1935), *Practitioner*, **135**, 312.
THEOBALD, G. W. (1932), *Lancet* (ii), 1380.
BASHFORD, H. H. (1931), *Lancet* (ii), 1277.
SCOTT, W. L. (1937), *Lancet* (ii), 397.

Discussion.—The PRESIDENT said that Dr. Bashford had, at the Post Office, opportunities for investigation into the after-effects of disease of which he was taking advantage to answer many problems which remained unsolved by the textbooks. He would like to ask him whether the cases of albuminuria to which he had referred had cleared eventually, whether they were examples of adolescent albuminuria such as the late Dr. William Collier had described in rowing men at Oxford thirty years ago, or whether they were ever followed by chronic nephritis. With regard to tuberculosis he knew that the Post Office Authorities took especial interest in the treatment of this disease; they had their own sanatorium. The results which Dr. Bashford had described tallied with general experience.

Dr. R. A. O'BRIEN said he hoped that Dr. Bashford would be able, with the aid of his unparalleled opportunities of following life histories, to decide in the next ten years whether a positive Mantoux response in young adult life was an advantage or a liability. At least one hospital superintendent had said that he would not take into his hospital a nurse who was Mantoux-negative.

Dr. G. CLARK TROTTER, referring to the prevailing tendency now to shorten or do away with the period of quarantine in the case of workers, said that the enforcement of a set period of absence because of a case of infectious disease in the house was unnecessary except in special circumstances. The worker might, generally speaking, be allowed to return to work if the infectious case had been removed to hospital and disinfection carried out, and in large public health departments this method was now followed. It entailed supervision of the premises, of course, and a warning to note any signs of approaching sickness in other members of the household. As a rule secondary cases in adults were rare.

He was especially interested in the remarks on those nearing a possible retirement age, whose minor ailments were made an excuse for prolonged absence. He might instance an experience of his own when he was acting for the Post Office in a country district many years ago, when a man had sickness clubs which, together with his sickness allowance, brought in a fair sum and made him relatively better off when he was away from work. He thought that the advent of National Health Insurance and a decline in these clubs was the reason why there was less "malingering" than formerly.

Major J. S. K. BOYD said that in the Army the use of anticatarrhal vaccine on a large scale had been given up. Attempts to protect troops against colds by this means had proved unsuccessful. Nevertheless, certain individual cases seemed to find benefit from the use of the vaccine, and proved their faith by returning regularly year after year for re-inoculation.

Dr. D. C. NORRIS, referring to the influence of age on the duration of disability, said that figures had recently been published ("The Evaluation of Permanent Incapacity for Work in Social Insurance", p. 177, International Labour Office, 1937), showing that in the experience of the Scottish Health Insurance Scheme officials, in 1934–35 the average disability was twenty-seven days for men aged between 20 and 25, forty-one days for those between 40 and 45, and one hundred and sixty days for those between 60 and 65. Had Dr. Bashford found as great a disproportion as this, amounting to about 6 to 1 in the case of the older workers?

Dr. Bashford had described the way in which minor neuroses were successfully dealt with by a "straight talk" in a single interview. What was his practice in dealing with really serious cases of anxiety neurosis? Did he advise treatment by a psychologist? The chief difficulty in providing such treatment was its high cost—perhaps £50 to £100 per patient. It would be interesting to hear whether Dr. Bashford had found that such disabling neurosis tended to occur particularly among persons in senior grades, holding posts of considerable responsibility.

Dr. BASHFORD (in reply to the President) said that in no case had chronic nephritis been observed to follow in the group of adolescent albuminuria subjects quoted.

In reply to Dr. R. A. O'Brien he said that, with the consent of the Post Office, of the relative Staff Associations—and, where necessary, with parental consent—a group of volunteers in the Post Office were being examined in respect of the Mantoux test under the ægis of the Prophit Research and the Royal College of Physicians.

In reply to Dr. G. Clark Trotter, he would reaffirm the extreme rarity of true malingering in his own experience. In reply to Major Boyd: When individual Post Office medical officers wished to prescribe anticatarrhal vaccine in particular cases, facilities for this were always given. In reply to Dr. J. C. Norris: Where expert psychological treatment was available appropriate cases were referred for it.

CORRIGENDUM

Vol. 31, p. 35 (Section of the History of Medicine, p. 9, President's Address)

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THE PRINCIPLE OF BIOLOGICAL OR CONSTITUTIONAL TREATMENT

Section of the History of Medicine

President—A. P. CAWADIAS, O.B.E., M.D.

[*November* 3, 1937]

The East India Company and the Control of Scurvy

By J. A. NIXON, C.M.G., M.D.

FROM 1601 onwards the East India Company's ships carried a supply of oranges and lemons, or lemon juice, for the prevention of scurvy amongst their crews. By the kindness of Mr. Ottewill (Keeper of the Records at the India Office) I have been made aware of the complete knowledge which the Company possessed at that early date of the prevention and cure of scurvy.

So far as I can ascertain, the man who was responsible for introducing the remedy to the Company's ships was Sir James Lancaster, who sailed as Commander of the first fleet sent by the Company to the East Indies in 1600. Grant, in his book *The East India Company*, described Lancaster as a " tried seaman who had been employed some years before in the conduct of a privateering expedition to the East Indies." This " privateering expedition " is included in Hakluyt's *Principal Voyages of the English Nation*, " A Voyage with three tall ships . . . to the East Indies by the Cape of Buona Speransa . . . begunne by M. George Raymond in the yeere 1591 and performed by M. James Lancaster and written from the mouth of Edmund Barker of Ipswich, his lieutenant in the sayd voyage by M. Richard Hakluyt ". In this account there are several references to scurvy in the ships. On the return journey they set sail on " the eight of December 1592 " because the men said " that they would take their direct course for England and would stay there (Point de Galle in Ceylon) no longer ", and " the Captaine was constrained to give his consent to return ".

At St. Helena it is recorded that one man " was diseased with the skurvje " but he and another who " had bene nine moneths sick of the flux, in short time while

they were on the Iland recovered their perfect health. We found in this place great store of very holesome and excellent good greene figs, orenges and lemons very faire, abundance of goates and hogs and great plenty of partriges, guiniecocks and other wild fowles ".

From St. Helena they crossed the Atlantic and touched at several of the West Indian islands, running short again of provisions but ultimately reached Rye on " the 24th of May 1594 ".

Apart from the reference to fresh fruit at St. Helena which is not specifically mentioned in Barker's account as being anything more than part of the fresh provisions found on that island, there is nothing to indicate that Captain Lancaster was able to keep his crews free from scurvy nor that he recognized the superior value of oranges and lemons as a remedy.

Yet when one reads the account in *Purchas his Pilgrimes* of " The first voyage set forth by the East India Company in 1600 " it is evident that Lancaster had a sound grasp of the prevention and cure of scurvy. Purchas describes how the fleet arrived at Soldania (from a note in Markham's *Voyages of Sir James Lancaster*, Hakluyt Society 1877, this would appear to be Table Bay) with much scurvy in the ships. The narrative goes on " The generall (i.e. Lancaster) went aboord them and carryed good store of men. . . . The reason why the generall's men stood in better health then the men of the other ships was this :

" he brought to sea with him certaine bottles of the juices of limons, which he gave to each one as long as it would last, three spoonfuls every morning fasting not suffering them to eate anything at all after it till noone. This juice worketh much the better if the partie keep a short Dyet, and wholly refraine salt meate, which salt meate, and long being at sea is the only cause of the breeding of this disease. By this meanes the Generall cured many of his men and preserved the rest ".

A little later another reference to scurvy occurs : " and to strive long in hope of change of windes wee could not for now our men began againe to fall sicke of the scurvy. Then the Captaine of the Vice-Admirall called to the Generall and thought it best to bear into the bay of Antongile and there to refresh our men with oranges and lemons, to cleere ourselves of this disease ".

One more reference is to be found : " (We) sent our Boats aland to Saint Maries where wee had some store of limons and oranges, which were precious for our diseased men, to purge their bodies of the scurvy ".

Lancaster's knowledge was quickly applied by the Company so that the supply of fresh oranges and lemons and lemon-juice became official.

In the *First letter-book of the East India Company* 1600–1619 this entry appears :—

" A computacion of the chardge for setting forth to sea upon a third voyadge to Bantam and the Moluccos . . . with the *Dragon*, *Hector* and a pinnace ". In this computation there is an entry of " lemon water " among " the p'portion of victuals for the two shippes and the pinnace with 280 men ". The editors of the *First letter-book* (Sir George Birdwood, Surgeon, and Sir William Foster, Head of the records) added a footnote " We may trace in this item the hand of Sir James Lancaster who was one of the first to use the juice of lemons as an antidote to scurvy . . . not formally adopted by the Admiralty until 1795, nearly two centuries after its value had been pointed out by Albertus and its practical efficacy demonstrated by Sir Richard Hawkins and Captain Lancaster ". I cannot understand why Albertus is placed in the same category with Hawkins and Lancaster. In his *Schorbuti Historia* published in 1594 Solomon Albertus mentions the value of fresh food generally,

including domestic poultry such as fowls and pigeons or wild fowl, as well as pheasants and partridges which he advises cooking with oranges or orange juice ; elsewhere he recommends various fruits and herbs. But as there is little in the Pharmacopœia of those days which he does not recommend he cannot be said to rank with Lancaster in having singled out oranges and lemons.

In the *Hawkins Voyages* (Hakluyt Society, 1878) there are published " The observations of Sir Richard Hawkins, Knight, on his Voyage into the South Sea ". Scurvy is fully described in Section XVI. He recommends scrupulous cleanliness of the ships, of the men, and of their clothes, together with "exercise of work, of agilitie, of pastimes, of dancing, of use of armes " ; also " a morning draught of wine or beere ".

He concludes : " That which I have seen most fruitful for this sicknesse is sower oranges and lemmons, and a water which amongst others (for my particular provision) I carryed to the Sea, called Dr. Stevens his water ". . . .

In this voyage in 1590 Hawkins lay becalmed " nearly 6 months with a fleet of Her Majesties' ships about the ilands of the Azores ". He relates how " many of every ship (saving of the *Non-pareil*, which was under my charge and had only one man sick in all the Voyage) fell sick of this disease (i.e. Scurvy) and began to die apace ".

Again when he sailed on the *Dainty* to Brazil he says " that the sicknesse of my people made mee to seeke the shore ". He put into Santos, now known as Victoria, a Brazilian port in the Bay of Espirito Santo, when the Governor procured for them " two or three hundreth oranges and lemmons and some few hennes ".

There is no doubt that Hawkins was as well aware as Lancaster that oranges and lemons were the best cure or preventive for scurvy.

I raised the question with Mr. Ottewill whether it could be established that the East India Company supplied oranges and lemons to their ships as a regular practice. He showed me in the *Letters Received by the East India Company from its Servants in the East* a letter of complaint from Captain Keeling who sailed in command of the Third Voyage with the *Dragon* and *Hector* mentioned above. This letter is dated 19th June 1615 and is couched in a tone which leaves no doubt that he was bringing to the Directors' notice a dereliction or oversight which he judged they would not condone.

" Your lemon water in that fleet stark naught, a complaint of the Portuguese and the fleet generally ". The phrase " your lemon water " seems to mark it as an authorized item in the victualling of the fleet.

One more book was produced by Mr. Ottewill in proof of his contention. *The English Factories in India* 1630–33 contains (p. 42) Nicholas Sharp's account of the Homeward Voyage of the *Charles* (*Marine Records*, vol. 53, p. 25) : " July 14. The fleet from England arrived and landed their sick men ; but having no orugings (*sic*) and lemons were not recoveried, but something better than they were ". This reads as though Nicholas Sharp expected the ships to carry oranges and lemons in their stores.

Lind quotes Purchas's description of Lancaster's voyage with its clear emphasis of the importance of oranges and lemons, but he lays no stress on these particular fruits.

Hess, in his book on Scurvy (Chapter VI : Historical Review) appears to misquote Lind's version of Lancaster's voyage ; Hess gives the version : " In the year 1600 four sailing vessels left England for the East Indies. The sailors on three of these ships

did not receive lime juice, whereas those on the fourth received their daily quota. The men of the first three ships suffered severely from scurvy, but those on the fourth escaped ". This is a sorry curtailment of Lind who gives Purchas's account verbatim and never mentions *lime* juice at all—nor did Purchas. The phrase was explicitly " the juice of lemons ".

Budd, writing the article on Scurvy in Tweedie's *System of Practical Medicine* puts the whole of the early history accurately and clearly : " The efficacy of oranges in preventing and curing scurvy was discovered before the disease had been described by physicians. Ronsseus, one of the earliest writers on scurvy, in a work published in 1564, observes that seamen in long voyages cure themselves of it by the use of oranges. He conjectures that Dutch sailors, afflicted with scurvy on their return from Spain with a cargo of these fruits, had by chance discovered their efficacy.

" Albertus, in a treatise on scurvy, published in 1593, recommends the juice of oranges, and of sour and austere plants. He advises that this juice should be put into soups, and that meat, while roasting, should be sprinkled with it. In the same year, the virtues of lemon-juice in the cure of scurvy were experienced by Sir R. Hawkins, whose crew, while within the tropics were affected with it in an extreme degree.

" We have already given an instance of the extraordinary efficacy of lemon-juice as a preventive of scurvy, in the first voyage for the establishment of the East India Company in 1600. After this it seems to have been pretty generally used in the Company's ships ; and, in a medical work published in this country in 1636, it is recommended as the best remedy for scurvy. . . .

" Most of these proofs of the efficacy of oranges and lemons were collected by Dr. Lind, and published in his justly celebrated work on scurvy in 1757. His earnest recommendation for the general employment of these fruits in the Navy was, however, not acted upon for some time ; the disease continued to depopulate our fleets, offering a striking example of the delay which sometimes attends the practical application of most important truths."

Once again Hess is guilty of a mis-quotation. He states that Budd tells us that " in the sixteenth century sailors of a Dutch sailing vessel laden with these fruits were attacked with scurvy, and that, when they partook of the lemons and oranges in the cargo, a miraculous cure resulted ". This is not what Budd wrote. He quotes this statement as a conjecture of Ronsseus.

It is difficult to see how this knowledge of the value of oranges and lemons did not spread from the East Indiamen to the Navy. I ventured to suggest to Mr. Ottewill that possibly the Company kept the remedy a close secret, but he pointed out that it had been published by Woodall in 1628.

Despite occasional references to the value of oranges and lemons such as occur in *Ives's Journal*, 1745 (quoted by Lind), where he says that he gave " to every scorbutic patient one China orange and three apples ", and Lind's advice that lemon juice can be prepared and stored for long voyages, as Lancaster had shown, it was not until Captain Cook's voyage in 1769 that the Royal Navy adopted this means of preventing scurvy.

Even then it was misunderstood, and very often the juice of West Indian limes was provided with disastrous results. The story of Scott's voyage to the Antarctic, and of the Mesopotamian Expeditionary Force demonstrate how long it was before the value of Lancaster's experience and of the practice of the East India Company was fully appreciated.

Woodall's references in his *Surgeon's Mate* are as follows :—

" Further, the chirurgeon or his mate must not fail to persuade the governor or purser in all places where they touch in the Indies and may have it to provide themselves of juice of oranges, limes, or lemons, and at Banthame of tamarinds."

" And note for substance, the lemons, limes, tamarinds, oranges, and other choice good helps in the Indies which you shall find there do far exceed any that can be carried thither from England ; and yet there is a good quantity of juice of lemons sent in each ship out of England by the care of the merchants, and intended only for the relief of every poor man in his need, which is an admirable comfort to poor men in that disease."

" The use of the juice of lemons is a precious medicine and well tried, being sound and good, let it have the chief place, for it will deserve it."

" Some chirurgeons also give of this juice daily to the men in health as a preservative, which course is good if they have store ; otherwise it were best to keep it for need."

Woodall was born about 1569 and, at the age of 20, served in Lord Willoughby's expedition to render assistance to Henry IV of France. He then travelled for many years in France, Germany, and Poland, living by the practice of his profession until his familiarity with the plague tempted him to settle in London during the great plague year, 1603. Shortly afterwards he was appointed Surgeon-General to the East India Company, and in 1616 he became surgeon to St. Bartholomew's Hospital. He was appointed in 1627 to go to Portsmouth to cure the wounded soldiers that came from the Isle of Rhé in France. He died in 1643.

The Latin text of Ronsseus, with a translation, is appended.

Ronsseus. Epist. II. *On Scurvy.*

Nam et ea, quae secundum methodum sunt, omittamus, novimus nonnullos, qui solo pomorum aurantiorum unà cum corticibus usa sanitatem recuperarunt. Quod etsi empiricum sit, cum ipsa tamen ratione nonnihil habere commune videtur, siquidem quum in lienis affectibus, authore Galeno, opus sit attenuantibus pharmacis, citra manifestam aliquam caliditatem, cum modica astrictione, ut robur addatur affectae particulae, aurantia affecto lieni non prorsus inutilia pronunciabimus. Incidunt etenim, compescunt aestuantem sanguinem, & robur addunt laesa parti. Caeterum num ratione duce, homines barbari, ad propellen dam hanc luem aurantiis primum usi fuerint, pro incomperto est : mihi probabilior ea videtur opinio, quae fortuitò, & casa quopiam facultatem hanc compertam esse asserat, redeuntibus ex Hispania Batavis nautis, ac uberi novitate aurantiorum allectis, praeter spem avida quadam gulositate morbum pellentibus, atque id non semel felici successu experientibus.

Translation :—

For to say nothing of the remedies regularly employed in practice, we know of some people who have recovered health solely by taking oranges, skins and all. Although this is empirical it seems to have something in common with reason, for inasmuch as in diseased spleens we need, on Galen's authority, reducing drugs without obvious heating qualities, together with moderate astringent action so that the affected part may be strengthened, we shall

pronounce oranges not wholly useless in a diseased spleen. For they put an end to and check the excessive flow of blood, and give strength to the affected part. Still, it cannot be ascertained whether barbarians, guided by reason, first used oranges to ward off the disease ; to me the more probable opinion seems to be that which maintains that this property was discovered accidentally and by chance by some Dutch sailors returning from Spain who were attracted by the novel richness of oranges, and by their greedy gluttony unexpectedly drove out the disease and had this happy experience not once only but repeatedly.

Section of Comparative Medicine

President—S. P. BEDSON, M.D., F.R.S.

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DISCUSSION ON RECENT WORK ON HEAVY PROTEINS IN VIRUS INFECTION AND ITS BEARING ON THE NATURE OF VIRUSES

Dr. J. Henderson Smith: There is nothing new to the plant pathologist in the idea that virus is associated with crystals. Iwanowski pointed out over thirty years ago that tobacco mosaic disease was characterized by the appearance in the cells of flat plate-like crystals which were not found in the cells of normal plants, and these exhibited marked cross striation, especially under the action of acid. It was not then suggested that these crystals were anything more than a regular concomitant. Very much later (in 1931) when attempts were being made to obtain virus in a purified state, freed from the non-specific ingredients of the plant juices, the idea was mooted that the virus itself might be crystalline. True crystals which had infective properties were in fact actually obtained, and the conception of a crystalline virus became familiar. But these crystals were soon shown to be really crystals of the phosphate used in the method of purification, and their infectivity was due to virus entangled as they formed. It was not till about two years ago, when Stanley brought out his paper on "The isolation from diseased tobacco plants of a crystalline protein possessing the properties of tobacco mosaic virus" that the possibility of a genuine crystalline virus had to be seriously entertained.

This conception was abhorrent to the average biologist, who had looked on a virus as a living thing, and was convinced that there is a sharp demarcation between the living and the non-living. For many years nothing was known about viruses that was definitely incompatible with the view that they were essentially living organisms, rather like small bacteria—very small, since they were filtrable, and with special properties associated with the large surface they possessed relative to their bulk. They were obligate parasites, and it was thought that because of their small size their food had to be prepared for them by the host; but apart from that condition of their existence they were organisms like any other organism. They varied in size in a descending scale, but even when so small that they could be photographed only by short wave-length light they looked like organisms. With further research, however, the position became rather difficult to maintain. Elford's gradocol membranes showed that some at least of the viruses were smaller in size than single molecules of known proteins, such as the hæmocyanins, and Laidlaw found a sewage organism,

whose dimensions entitled it to the name of virus, but which grew on artificial or at least cell-free media. It was difficult to believe that a thing the size of a single molecule could possess all the properties of life—whatever that may mean. The diehard vitalist began to feel that his position was not so secure as he had believed.

Then Stanley claimed to have isolated a crystalline protein with all the properties of the tobacco mosaic virus. The assertion that the virus was crystalline was responsible for much of the attention at first given to the new claim, for those of us who had been brought up in the older order of ideas attached a kind of sanctity to the word "crystal". It was a kind of guarantee of purity, and Stanley himself cited as evidence of the purity of his protein the fact that it could be recrystallized as many as 15 times without change of properties. Whilst Stanley was working on tobacco mosaic, Bawden and Pirie in Cambridge had been isolating virus proteins from plants infected with potato mosaic. The potato mosaic viruses do not give, or at least have not yet given, the needle fibres, but when Bawden came to Rothamsted and applied to the tobacco mosaic virus the methods used on potato, the same needle crystals as Stanley's were obtained, and most of his results were confirmed. The highly purified proteins, however, were shown to give liquid crystalline solutions, and it was suggested that the needle structures were not true crystals. Bernal has now shown that they are not really crystalline in the old sense of the word, but have a 2-dimensional regularity instead of a 3-dimensional, and are better described as fibres or paracrystals. It was also shown that their repeated production is no guarantee of purity. But the crystalline property attributed to tobacco mosaic undoubtedly caught the attention of many who might otherwise have been slow to appreciate the significance of the new step.

I do not propose to go much into detail, or touch, except incidentally, on the animal virus work. I will give only the broad outline of the progress made to date on the plant side, taking tobacco mosaic virus as the chief example.

There is no doubt that the material isolated from the juice of infected plants has most of the properties of tobacco mosaic. It is infective in concentrations of the order of one hundred-millionth of a gramme per c.c., increases very rapidly in the infected plant, and is transmissible in series indefinitely. The disease produced is identical in every respect with the disease of the plants from which the material was obtained in the first instance. With one important exception—with which I will deal in a moment—it has all the properties of the virus found in naturally infected plants, such as resistance to chemicals, ageing, heat, enzymes, &c.

There is also no doubt that it is a protein. It gives all the usual reactions, and its analysis conforms to that usual in known proteins. Bawden and Pirie consider that it is a nucleoprotein, but the American workers do not accept this view. The discrepancy is important, because of the implications and associations which a nucleoprotein-nature suggests, but that is a technical matter and will no doubt soon be cleared up. Its composition is constant, whatever the source of the material analysed and the concentration of the substance it contains. It can be obtained from every host plant that the virus can actively infect. It is, therefore, not a substance peculiar to the tobacco plant or the tobacco virus complex, but appears wherever the virus is able to multiply—even in hosts in no way related to the tobacco plant, such as phlox or spinach.

It has not been found in any normal plant, even in very small amounts, and the methods of extraction are delicate enough to reveal it, even when it constitutes only a millionth part of the plant tissue. In the infected plant, on the other hand, it occurs in surprisingly large quantities. The juice of an infected plant contains from five to ten times as much soluble protein as that of a normal plant, and about 80%

of this soluble protein consists of the abnormal substance. From one to two grammes can be obtained from a litre of sap, the amount varying with the condition of the infected plants and the duration of their infection. Where all this excess protein comes from is unknown. It is conceivable that it is a modification of the protein already existing in the normal plant. Possibly the existing protein, perhaps the non-soluble portion, is converted into the new soluble form, and the cells, requiring the normal protein for their own purposes (and one must remember that the diseased plant, though damaged, is still a functioning organism, growing to a large size), are stimulated to replace the converted material by more of the original, which is in its turn converted; and so we get an accumulation of the new form, giving a total content of soluble protein much greater than is normally found. There is indeed a small bit of evidence that there is actually less of the normal protein in the diseased plant than in the normal plant. This theory would imply that the creative force, the synthetic or constructive power which converts the normal material into the abnormal, resides in or is a property of the abnormal substance itself. But there are other obvious possibilities. It may be, for example, that the *cell* produces the abnormal protein under the stimulus of the abnormality, a theory which dodges the necessity of giving reproductive powers to the protein itself. The plain fact is that we have as yet no evidence at all as to the mechanism or the source of this huge development of a foreign substance.

From solutions of the protein can readily be obtained needle-shaped bodies resembling crystals, which are easily visible under the microscope. They average in length about two- to three-hundredths of a millimetre. They can be easily dissolved and again obtained, and the process can be repeated indefinitely. In spite of this it has been shown by Bawden that these "crystals" are not necessarily pure, even after repeated recrystallization but, as ordinarily prepared by precipitation with ammonium sulphate, contain a fraction which is not virus protein and can be removed by tryptic digestion. This has been beautifully demonstrated by the anaphylactic reaction by Chesters, who showed the presence of the impurity in the American ammonium sulphate crystalline protein, and its absence in the purified material prepared by Bawden.

These crystals are not true crystals in the ordinary usage of the term. They should rather be described as fibres or paracrystals, and under certain conditions the protein can be obtained in the solid form as long mesomorphic fibrils visible to the naked eye. These have the orderly molecular arrangement found in crystals, but so have many other things, such as muscle fibres or hair structures. They have a 2-dimensional regularity instead of a 3-dimensional, and the use of the term crystalline is misleading, at least to those who are not familiar with the modern extensions of this word. That they are better described as fibres is shown by the mode of their formation, which consists in the breaking-up of a gel into slivers or splinters.

When a solution of the protein reaches a certain concentration it reveals a new property, becoming birefringent and showing anisotropy of flow. This property indicates that the constituent particles are rod-shaped. When the concentration is high, so that the rods cannot move about freely but are necessarily arranged in parallel bundles owing to lack of space, the solution is permanently birefringent. When the concentration is of a lower order, the rods are able to move comparatively freely, but on the formation of currents or eddies they assume the parallel orientation, and there is anisotropy of flow. The property is greatly affected by impurities, notably by the presence of breakdown products of the virus protein, and it is not possible at present to estimate the length of the rods with any precision, though it seems that this must be at least ten times as great as the width. The width can be estimated accurately from X-ray analysis. This will be discussed by Bernal later

on, and I will not anticipate his remarks further than to say that the cross diameter is 150 Ångströms, that the cross sectional area amounts to 20,000 square Ångströms, and is probably triangular, and that these dimensions are constant for all concentrations of the protein.

The molecular weight and the particle size could be derived from the sedimentation constant if the particles were spherical. Since they are rod-shaped, it is scarcely possible to arrive at a really reliable value for the particle size. The cross-section shows that the molecular weight is large, and if we take the length as ten times the width and the specific gravity as 1·37, the minimum molecular weight must be of the order of 20 millions—not grossly different from the 17 millions calculated by Svedberg for the American preparation. This is enormous. It is larger than the largest hæmocyanins, and is approached by only one known substance, a thyroglobulin polymer, which is estimated to have a weight of 15 millions. The new protein is, at least, a very unusual substance—unlike anything found in the sap of normal plants.

There is reason to believe that these rods are not the ultimate constituents, but are aggregates of sub-units arranged in linear form. The chief evidence for this is the fact that in the purified state the protein has lost the outstanding character of a virus, namely filtrability. Every operation which precipitates the protein, such as simple high-speed centrifugalization, precipitation by alcohol, by acid, or by ammonium sulphate, entails this loss of filtrability. We know that in untreated sap the virus can be filtered through membranes of a pore size of 53 mμ, but when the virus is purified, it will no longer pass a membrane with 450 mμ pores. It looks as if in the juice, and probably in the living plant, the virus exists in a smaller and more discrete form, but in the isolated condition it has undergone an aggregation or polymerisation. The aggregation must be linear, because its width remains the same. The fact that such rods of unaltered width do not pass the filters endways on is perhaps a phenomenon similar to the jamming of logs when lumber is being floated down a river. There is other evidence that in the crude sap the protein is present in a different molecular arrangement—for instance, the absence of anisotropy in sap which is a solution of 0·2%, and the smaller infectivity of the isolated virus, whose serological titre nevertheless remains the same as that of the virus in the sap. Up to the present it has proved impossible to disaggregate the protein by any method tried.

Proteins of this type have now been isolated by Bawden and Pirie from three strains of tobacco mosaic and two strains of cucumber mosaic having a serological affinity to tobacco mosaic. The diseases are clinically distinct, and the corresponding proteins are also characteristically distinct. The protein varies as the virus varies. From other diseases, such as certain of the potato mosaics, these workers have obtained infective nucleoprotein precipitates which are amorphous and do not give the needle crystals, and which have a different composition on analysis. These proteins are susceptible to tryptic digestion and so cannot be purified by its use, but they can be obtained by high-speed centrifuging. Other viruses examined in America have yielded similar proteins. But we have no reason to suppose that all viruses, even all plant viruses, will conform to any of the types as yet investigated, and it is unwise to generalize from the small number examined. All we can say is that so far the viruses examined *have* given infectious proteins with the properties I have been describing.

There remains now the question—is this protein actually the real virus, the *virus ipsissimum?* If we could be quite certain that the purified protein is really homogeneous, really pure, the question would not arise. So far as we have been able to determine, virus proteins have been prepared which do seem to be really homogeneous,

but it can always be asserted that they are not, and that the virus is present as an impurity in the protein preparations. Although the protein is found only when the virus is found and is specific, it may yet be a reaction product produced by the plant in response to the virus, a symptom in fact just like any other symptom, and its infective properties are due to the presence in it of the true virus, from which it has not yet been separated. This theory cannot be directly disproved for one remembers the presence of argon in what was believed to be pure nitrogen and of heavy water in pure water. Moreover, there is always the possibility that some test as yet unthought of, or some increased refinement of the existing tests, may reveal such impurity. This theoretical possibility must always remain, but the mass of evidence against it is now so large that we are entitled to disregard it and the onus of proving its existence as a fact is transferred to those who assert it.

Certainly there can be no gross impurity or inhomogeneity. The constancy of the product obtained from the most varied sources is enough to show that much; and also the infectivity, which is regularly demonstrable in a concentration of 10^{-8} to 10^{-10}. Neither test is very refined. Analysis would not reveal an impurity of less than 1%, and the infectivity test, owing to the variability of the test plants and the unavoidable uncertainty as to the exact amount of effective inoculum, leaves a considerable margin of variation. It is affected, too, by the difference in the molecular state in the sap and in the isolated protein, and this makes precise comparison between the infectivity of the sap and the protein impossible. We can, however, be sure that the protein is many times more infective than the original material.

Any procedure that removes protein lowers the infectivity, and the activity declines *pari passu* with degradation of the protein. The temperature or the degree of acidity or alkalinity which destroys the protein, also destroys the activity, and it has not been found possible in any way to dissociate the protein from the virus. The hypothetical virus contaminant must have the same iso-electric point. It must also have the same molecular weight, since in the analytical centrifuge the pure protein gives the sharp sedimenting boundary of a single molecular species. In short, the contaminant must have the same physical properties as the protein, and, applying the razor of Occam, it is gratuitous to postulate the presence of two substances where one is enough to satisfy the data.

So far as can be seen at present, the evidence is all in favour of the view that the protein is the actual virus, and whatever the implications involved one must proceed on that assumption.

Dr. C. H. Andrewes: Workers with viruses pathogenic for animals—animal viruses, for short—must have watched with interest and excitement the recent work on plant viruses, and must have wondered how far the results would be applicable to their own subject. My part in this discussion is to review the work so far published on " heavy proteins " in animal virus infections. As yet there is little to review—only a few short notes by Wyckoff and Beard.

These authors, working at Princeton in close contact with Stanley, first studied the virus of the rabbit papilloma (Shope), a virus remarkable for its great resistance to heat and other agents. Suspensions of warts were purified by repeated fractional centrifugation in the ultracentrifuge, coarse particles being deposited at low speeds and discarded, and then the virus bodies thrown down at high speeds and repeatedly washed. Beard and Wyckoff (1937) thus obtained suspensions of bodies which, from the evidence they offer, almost certainly represented the active agents of the papilloma. When observed by means of the Svedberg optical apparatus in connexion

with their ultracentrifuge, the bodies were found to deposit in a manner indicating great uniformity in size, the particle size corresponding to a molecular weight of 20 million or a diameter of 40 mμ, a figure which agrees well with that obtained by filtration. The material gave the chemical reactions of a protein and contained 15% of nitrogen. Beard and Wyckoff concluded that they had obtained a "high molecular weight protein with which is associated the infectiousness of the disease".

This sounds dramatic, but I wonder if it really means much. May it not be that the novelty of the conclusion lies not so much in the technique or in the experimental results, as in the attitude of mind of the workers? If we ourselves should carry out washings of a virus in a centrifuge and find that our deposit consists of bodies of uniform size giving the chemical reactions of a protein, we should state that we have obtained a suspension of purified virus bodies, which contain protein, and nobody would give us credit for having done anything important. If, however, we called our product a high molecular weight protein, we should produce a profound impression on the scientific world.

Later, Wyckoff (1937) carried out similar experiments with the virus of equine encephalomyelitis, and found that it deposited about as readily and as uniformly as that of the rabbit papilloma. The molecular weight of this heavy protein was estimated as 25 million. As this virus is very unstable at room temperatures, all manipulations had to be carried out in the cold; the virus rapidly disintegrated on standing, and the uniformly sedimenting particles shown by the Svedberg optical system were no longer recognizable. Further observations on the sedimentation of the rabbit papilloma (Wyckoff and Beard, 1937) now revealed that at a pH of 10 on the alkaline side and 3 on the acid side the virus-heavy protein broke up into smaller fragments; these points correspond with the pH values at which infectivity of the virus was very rapidly lost, though it is true that virus held between pH 7 and 10 was slowly inactivated though its sedimentation constant was unaltered. Experiments of this sort are clearly likely to yield information of great interest, though in the present state of knowledge I do not think that they justify definite conclusions about the nature of viruses.

Beard, Finkelstein, and Wyckoff (1937) have quite recently carried out similar experiments with vaccinia virus—a virus whose diameter is about five times that of the two previously studied. Again particles sedimenting in a very uniform manner were obtained, and it was again found that this uniform sedimentation was only to be observed over a pH range in which the infectivity of the virus was well preserved. I do not know whether these workers conclude that vaccinia virus also is to be described as a "heavy protein". If uniformity of sedimentation and positive chemical tests for proteins are the sole criteria, presumably they should logically do so. Possibly they hesitate because Hughes, Parker, and Rivers (1935) found that their preparations of vaccinia, purified by similar means, contained, in addition to protein, some fat and also carbohydrate which was readily washed away.

Workers with animal viruses have made valuable progress on the basis of a working hypothesis that viruses are micro-organisms owing their peculiar characters first to their small size and secondly to their highly specialized intracellular parasitism. What is to be their attitude in view of the recent work on heavy proteins, particularly in relation to plant viruses? They may, I conceive, adopt one of four attitudes:—

(1) They may disclaim any interest in botany, holding that the work on tobacco mosaic has no bearing on their own problem. There seems no logic in this; the most important properties of viruses appear to be held in common by those attacking animals and those attacking plants.

(2) They may suspend judgment pending further proof that the crystallized product really represents the virus. This attitude is more reasonable. At first the identity of the crystals and the virus seemed very doubtful, but the evidence in its favour is in my opinion gradually increasing.

(3) They may abandon their defences and cease to think of viruses as micro-organisms and regard them as auto-catalytic enzymes.

(4) They may hold that what Stanley has done is, after all, primarily to show that the infective particles of a virus under certain conditions arrange themselves in regular rows. In my opinion this fact does not solve the problem of whether they are micro-organisms or autocatalysts.

I shall not discuss whether these viruses are alive or dead, because I think it obvious that according to the criteria we have held in the past they possess some of the properties hitherto associated with autonomous living things and some hitherto associated with non-living chemical substances. But I should *not* conclude from that that they are in process of evolution from the non-living to the living. I find it far easier to think of them as small micro-organisms which in the course of evolution have gained by becoming smaller, losing some of the chemical complexities of larger beings, and perhaps thereby becoming subject to physico-chemical laws which may on occasion cause them to do such things as form paracrystals. I know that viruses are of a graded series of sizes, larger in some instances than cultivable organisms, that their immunological behaviour is like that of bacteria in that an animal once infected becomes more or less immune to subsequent infection, that some of them can form soluble haptenes, or multiply in an insect intermediate host, that they can mutate and adapt themselves to altered conditions. If I am asked to forget all that and adopt a new philosophy of life because the bodies in question can arrange themselves in orderly rows, I entirely refuse to do so.

REFERENCES

BEARD, J. W., and WYCKOFF, R. W. G. (1937), *Science*, **85**, 201.
BEARD, J. W., FINKELSTEIN, H., and WYCKOFF, R. W. G. (1937), *Science*, **86**, 331.
HUGHES, T. P., PARKER, R. F., and RIVERS, T. M. (1935), *J. Exper. Med.*, **62**, 349.
WYCKOFF, R. W. G. (1937), *Proc. Soc. Exper. Biol. and Med.*, **36**, 771.
WYCKOFF, R. W. G., and BEARD, J. W. (1937), *Proc. Soc. Exper. Biol. and Med.*, **36**, 562.

Dr. F. C. Bawden: It is extremely difficult to prove that something does not exist, and for this reason it is impossible for us to state dogmatically that the nucleoproteins we have isolated from virus-infected plants are the viruses themselves. Many substances long regarded as homogeneous have ultimately been shown to be heterogeneous, and it is well to begin by admitting the possibility that our purified virus preparations consist largely of an inert nucleoprotein contaminated with small amounts of active virus. There is no evidence at present to support this view, and I wish to give some of the reasons why we consider it to be improbable.

In the first place, the characteristic proteins which we have isolated have been found only in virus-infected plants, and they can be found in all species of infected plants, whether these are taxonomically related or not. An exhaustive search of healthy plants has not revealed anything at all similar to them, and the amount of protein that can be isolated from infected plants is directly proportional to the infectivity of the sap. Also, the particular protein isolated depends only on the virus used for infecting, and not at all on the host plant infected. This, of course, does not prove that the proteins are the viruses, for they may merely be specific by-products

of virus activity. If this view be adopted, however, the problem is greatly complicated, for the virus again becomes a mysterious something, with the added complication that it now not only itself increases but also causes the production of a specific and extremely unusual protein.

It has been known for some time that plants infected with certain viruses contain specific antigens, and a great deal of evidence has been accumulated indicating that the antigens are the viruses themselves. There can be no doubt that the nucleoproteins we have isolated are these specific antigens. One cubic centimetre of solution containing from one five-millionth to one ten-millionth of a gramme gives visible precipitates with antiserum, and the serological titres are therefore of the same order as those of other highly purified antigens.

Stanley describes the acid and ammonium sulphate precipitates from tobacco mosaic virus preparations as crystals, and argues that as repeated "recrystallizations" do not affect the properties his preparations are homogeneous. Even if the precipitated needles were true crystals it is doubtful if this argument is valid, but, although the protein possesses some properties that are characteristic of crystalline materials, the needles appear to be merely pieces of jelly containing 50% of water. They lack the 3-dimensional regularity of true crystals, and are more accurately described as fibres or as paracrystals. We have found that the appearance of the precipitated material is not greatly affected by the presence of comparatively large amounts of certain impurities, and the apparent physical uniformity cannot be taken as conclusive evidence of purity. We find that virus preparations which will not form dilute, spontaneously birefringent solutions can always be further purified, but when they do we have been unable to demonstrate any heterogeneity. Fractionations which often cannot be made by further precipitations with acid and ammonium sulphate can readily be made by incubation with trypsin. The further purification affected by this method is shown by some anaphylactic tests made by Chester, who finds that tobacco mosaic virus stimulates the production of good precipitating antisera but is not anaphylactogenic, whereas normal tobacco protein is strongly anaphylactogenic. Chester demonstrated the presence of normal tobacco protein by the anaphylactic test in all the preparations of tobacco mosaic virus prepared merely by precipitation methods, but he was unable to demonstrate the presence of such protein in our liquid crystalline preparations which had been treated with trypsin.

In addition to the virus causing ordinary tobacco mosaic, we have worked with the related strains causing Enation mosaic and Aucuba mosaic of the tomato, and with cucumber viruses 3 and 4. Although each of these viruses causes a characteristic disease, and the cucumber viruses have distinct host ranges, all five are serologically related. From different plants infected with each of these viruses we have isolated proteins which, when highly purified, form dilute liquid crystalline solutions. The analytical figures of these preparations are constant, and from the chemist's viewpoint they can probably be regarded as homogeneous. Dried preparations of all five viruses contain about 50% of hydrogen, 16% of nitrogen, 0·5% of phosphorus, and 2·5% of carbohydrate. When denatured by heating to 90° C. they all break down, and give a denatured protein free from phosphorus and carbohydrate, and a free nucleic acid of the ribose type. We have never obtained fully active preparations of any of these viruses free from nucleic acid, and we therefore describe our products as nucleoproteins.

Denaturation of the protein by heating, by acid, or by any other means, is accompanied by loss of virus activity, and the falling-off in the infectivity of a preparation is directly proportional to the amount of protein denatured.

The five viruses mentioned are obviously closely related to one another, and in any natural system of classification would be placed in the same group. The nucleo-

proteins isolated from plants infected with these viruses possess similar physical, chemical, and serological properties, but we have found sufficient differences between them to show that each is a distinct protein. Furthermore, the order of the differences between the proteins is that which might be expected from a knowledge of the pathology of the viruses, for the greater the differences shown by the viruses in their host ranges or in the symptoms caused, the greater are the differences that can be found in the serological reactions, X-ray diffraction patterns, and physical properties of the isolated proteins.

Recently we have been working with potato virus " X ", a virus not related to tobacco mosaic virus in any way, and very much less stable *in vitro* and more susceptible to most physical and chemical treatments. From plants infected with this virus we have also isolated nucleoproteins with a chemical composition similar to that of the tobacco mosaic virus. When highly purified, this nucleoprotein also forms dilute liquid crystalline solutions, and shows the phenomenon of anisotropy of flow quite as strongly as preparations of tobacco mosaic virus. When precipitated with acid and ammonium sulphate it does not give paracrystalline needles, but a flocculent amorphous precipitate. The properties of this protein differ from those of the tobacco mosaic protein in all the ways in which the two viruses are known to differ. Treatments which have no effect on tobacco mosaic virus, such as heating to 70° C., storing at pH 3 and incubating with trypsin, destroy this protein, and the destruction of the protein is again quantitatively related to the loss in infectivity suffered by the preparation.

There are many other reasons for thinking that the highly purified preparations of tobacco mosaic virus are relatively homogeneous. When they are centrifuged at high speeds sharp boundaries are given. The material also behaves uniformly in an electric field, and the X-ray patterns give no indication of the presence of more than one type of molecule. Also, the composition of the sediment is the same, whether the virus preparations are centrifuged at their iso-electric point or on the acid or alkaline side of it. Further, if the preparations were a mixture of virus and protein, it might be expected that precipitation with antiserum would alter the proportion of the components, but this does not happen. Protein which has been recovered from inactive mixtures with antiserum has the same chemical composition, and the same virus activity, as that obtained straight from the plant.

The virus in our purified preparations will not pass through fine filters, and this fact can be explained if it be assumed that the virus aggregates during purification, and it can be shown that the protein particles actually do aggregate. The amount of anisotropy of flow shown by a given weight of protein, other factors being equal, will depend on the length of the particles, for the longer the particles are in relation to their width the more easily will they be orientated by streaming. From the yields of protein obtained it is apparent that clarified infective sap is about a 0·2% solution, but the amount of anisotropy of flow shown by infective sap is much less than that shown by a 0·2% solution of the isolated protein in clarified healthy sap. This suggests that the particles in untreated sap are relatively small and that during purification they aggregate linearly to form long rods. One precipitation of the protein from sap is sufficient to bring about an increase in the anisotropy of flow, and this effect is always accompanied by a reduction in both the infectivity of the sap and the filtrability of the virus. That is, an observed aggregation of the protein is accompanied by changes in the virus which are readily explained on the basis of an aggregation of the virus particles. Yet another fact closely relating tobacco mosaic virus to the protein is that the width of the purified protein, as measured by X-rays, is almost identical with the width of the smallest virus particles in untreated sap as measured by the filtration end-point through collodion membranes.

At present we require about 10^{-10} of a gramme of tobacco mosaic virus protein to get an infection. Although the molecular weight of the protein is not known at all accurately, it is probable that this amount represents a large number of molecules. Our methods of inoculation are relatively crude, and there is no doubt a considerable wastage of inoculum, but until infection can be brought about by one molecule it is difficult to see how proof can be obtained that the proteins are the viruses. At the present stage of the work this seems most probable, and the results obtained suggest that it is reasonable to assume that if all the particles in our purified virus preparations are not active particles, they are at least similar to active particles in their superficial properties.

I would now like to say a few words about another aspect of the work on plant viruses which, if it can be applied to animal viruses, may be of some value in medicine. In doing this I do not wish to imply that I consider all viruses to be similar chemically, but some of the smaller and more stable animal viruses have properties in common with the viruses with which we have worked, and a claim has already been made that one animal virus has been isolated in the form of a protein. We find that any treatment which denatures the protein causes loss of infectivity, serological activity, and the characteristic optical properties. Certain treatments, however, destroy the infectivity of our purified virus preparations without affecting the serological reactions. These treatments do not denature the protein and have no effect on the ability of the virus preparations to form liquid crystalline solutions and to show anisotropy of flow. With plant viruses these results are of no practical value, but if they can be applied to animal viruses they may be useful in the preparation of vaccines. The methods which we find to be most effective are irradiation with X-rays and ultra-violet light, and treatment with nitrous acid, formaldehyde, and hydrogen peroxide.

Mr. J. D. Bernal: The optical and X-ray investigation of the virus preparations which Dr. Bawden has described answer at least some of the questions raised in the discussion. The physical properties of the majority of the viruses studied—i.e. tobacco mosaic, and cucumber and potato X-virus—all indicate the presence of long particles. These account for the double refraction of flow of the dilute solution, for the spontaneous double refraction of the more concentrated solution, for the formation of double refracting gels and also for the formation of the spindle-shaped tactoid bodies. These are formed as the result of the competing tendencies of surface tension to form a spherical aggregate and mutual orientation tending to form a linear one. There seems little doubt that the " crystals " originally described by Stanley are really microtactoids. We have shown that they are indistinguishable from the preparation we call " wet gel ", containing about 50% of water, formed by drying the concentrated solution. The X-ray evidence has confirmed these observations and added much new information. X-ray photographs of the virus show a pattern which may be considered in two parts : one of scattering at large angles, which corresponds to that of a semicrystallized protein, and one at small angles, indicating the packing of the particles. The latter has received more attention but perhaps wrongly so. The X-rays show unequivocably that the particles of the virus are practically identical and pack together in regular 2-dimensional bundles. There is no evidence of regularity in the direction of the rods themselves, but in the other two directions there is a perfect hexagonal pattern, the scale of which varies quantitatively with the amount of water that is inserted between the particles. The absence of 3-dimensional regularity is, however, probably fortuitous and due to the difficulties of inducing a higher degree of crystallization. Such a degree seems to be achieved in Nature, as true crystals containing the virus material, and probably other material

as well, are observed in the cells of affected plants, and these crystals possess end as well as side faces and undeniably show 3-dimensional regularity. This is, of course, no criterion of purity, especially as such crystals probably contain at least 50% of water ; indeed, Northrop has gone so far as to say that where proteins are concerned the larger the crystal the more impure the material.

If this were all the evidence, however, it would still be possible to claim that crystallization in this case was simply a packing together of essentially similar organisms, and did not involve anything incompatible with traditional views as to the vital nature of the viruses. It is the evidence of the large-angle scattering that makes this view untenable because here X-rays show unequivocally that regularities occur inside the particle. That these regularities belong to the particle is shown by the fact that they persist unchanged from the driest gel to the most dilute solution. The scale of this regularity is relatively small, of the order of 20 Å.—much smaller than any particle hitherto observed that may be claimed as a living organism—and is intermediate in character between that observed in undenatured and denatured protein patterns. If there is any more complex "vital" material about, it must be represented by only a small fraction of the bulk of the particles.

I should like to stress finally that the peculiar liquid crystalline character of the viruses hitherto studied, and also of bacteriophage, must be considered rather a convenient accident than an essential character. Quite recently Bawden and Pirie have obtained a preparation of the virus of the bushy-stunt disease of tomato, which shows no double refraction flow and produces isotropic rigid gels. The internal pattern, as shown by X-rays, proves, however, to be of essentially the same type as those of the other viruses, indicating that here, where the particles are not long but probably quasi-spherical and much smaller, a similar internal structure persists.

The physical and X-ray evidence can, of course, only tell us about the structure of the preparations which the biologists present us with ; whether they are or are not the virus we are not competent to discuss, but if on the ground of biological evidence they should be considered to be the virus, then the statements made as to their internal structure, though by no means final, must be taken as positive evidence for a high degree of internal and external regularity.

Dr. A. S. McFarlane : No one will disagree with Dr. Andrewes' criticism of the recently published work of Wyckoff and his collaborators, which is admittedly incomplete and does not in the end prove very much. Its weakness, however, does not justify bacteriologists in failing to realize the important implications of recent work on the heavy proteins. One main reason for regarding the animal viruses as living organisms is their high infectivity and ability to proliferate in contact with living matter. Now in one particle or molecule of tobacco mosaic there are a number of units—amino-acids or polypeptide chains—which are in the fixed relationship to each other of a crystal lattice. Crystallographic measurements indicate with a high degree of accuracy that there can be no significant amount of water inside each particle, and centrifugal results reveal a great similarity in the size of the particles. One could hardly imagine a state of affairs more unlike what would be expected if these particles were small organisms. Nevertheless, there has been a consensus of agreement by the previous speakers that these particles or molecules in contact with the living plant exhibit all the infectivity and proliferative ability which characterize viruses, and are in fact the virus. In my opinion this discovery casts more than a shadow of doubt on one of the central arguments for regarding the smaller viruses as living organisms. It would be very helpful to know more about the homogeneity in

size and the water content of the animal viruses. A reliable series of measurements of these two properties would no doubt go a long way towards solving the problem of where the heavy proteins end and miniature bacteria begin.

Dr. L. P. Garrod said that although the arguments adduced by Dr. Andrewes in support of the living nature of viruses were formidable, he ventured to suggest that one of them could be answered. This was the point that virus infections produced immunity, as bacterial infections did. Non-living substances could excite specific antibody formation, and it was not difficult to picture a precipitin-like action as the basis of acquired immunity to virus diseases, if the causative agent was in fact a protein. He had listened with great interest to Mr. Bernal's exposition; he wondered whether his description implied that the particles whose structure had been studied were single molecules.

Section of Neurology

President—ANTHONY FEILING, M.D.

CASES SHOWN AT THE WEST END HOSPITAL FOR NERVOUS DISEASES, WELBECK STREET, W.1, NOVEMBER 25, 1937.

Progressive Muscular Atrophy associated with Paralysis Agitans.—LEWIS R. YEALLAND, M.D.

Male, aged 61. Ten years' history of slowly progressive weakness, beginning in the right foot, then gradually extending to the other limbs. Four years' history of tremor.

Physical examination.—Extrapyramidal signs: Parkinsonian features with oscillations of the tongue, and "piano-playing" tremor of the fingers of both hands. Pyramidal signs: Double extensor responses. Lower motor neuron signs: Wasting of the hands and forearm, showing *main en griffe* and *main du prédicateur*; more or less generalized fibrillations and lost ankle-jerks. Tone: Flaccid in the upper and spastic in the lower limbs. Wassermann reaction negative in the blood and cerebrospinal fluid. The cerebrospinal fluid shows protein 0·12%.

Discussion.—Dr. YEALLAND demonstrated the clinical signs which he regarded as representing a combined lesion of striato-rubral, pyramidal and lower motor neurons. He said it was well known that there was often a lack of correspondence between the lesions and the clinical features of progressive muscular atrophy, inasmuch as the symptoms were usually confined to evidence of disease in the pyramidal and lower motor neurons, although other conducting pathways were found also to be pathologically involved without producing recognizable symptoms. He would welcome the views of members as to whether the lesion causing the progressive muscular atrophy had extended into the extrapyramidal system, or whether two separate diseases were present in this case.

After Cruveilhier, the history of progressive muscular atrophy had begun with Duchenne's description of a flaccid type. Charcot regarded a spastic type of the disease as a separate clinical entity and called it amyotrophic lateral sclerosis. The late Dr. James Collier held the view that the pathological background of the two was more or less identical. He (Dr. Yealland) thought that this patient was suffering from one disease—not from two

diseases—in spite of the fact that the clinical characteristics of each—i.e. progressive muscular atrophy and paralysis agitans—were conspicuously prominent.

The PRESIDENT asked what were the exhibitor's views on the explanation of the high protein in the cerebrospinal fluid.

Dr. J. R. GREENFIELD said that if this case were considered as one of amyotrophic lateral sclerosis, he did not understand why the ankle-jerks were absent without loss of power in the flexion of the ankle, nor why the upper limbs were flaccid when there was no loss of power in the upper arm. Was not this two diseases, or possibly two lesions, possibly on a vascular basis? He did not think this case fitted in with the picture of Charcot's amyotrophic lateral sclerosis. Moreover, the cerebrospinal fluid in that disease practically never contained an excess of protein.

Dr. YEALLAND (in reply) said that each of the pathways involved in this case exercised, when damaged, its own peculiar influence on the tone of the muscles. The tendency to flaccidity in the upper limbs and to spasticity in the lower limbs, he thought might be explained by the occurrence of a greater degree of degeneration in the ventral horn cells than in their corresponding pyramidal neurons in the cervical region; and by the occurrence of a lesser degree of degeneration in the ventral horn cells than in their corresponding pyramidal neurons in the dorsolumbar region. He did not know what influence the neurons belonging to a degenerated extrapyramidal system could exert on the muscles when the corresponding ventral horn cells to which the impulses ultimately converged were also degenerated, except in respect of the clinical features presented in this case. He was unable to suggest an explanation for the excess of protein in the cerebrospinal fluid.

Bilateral Ataxy with Rhythmic Tremor of Right Upper Limb.—LEWIS R. YEALLAND, M.D.

Male, aged 67. Two years' history of difficulty in walking, shaking of right hand, and shooting pains in the forearms. He has suffered from arthritis for many years and his hands show Dupuytren's contraction. The onset was gradual.

Physical examination.—Arthritis of right shoulder, wrists, and some of the hand-joints, with wasting and slight fibrillation of right supraspinatus and first dorsal interossei muscles. Rhythmic tremor, with rigidity, of right upper limb. Ataxy of arms and legs, not associated with loss of postural sense. Cranial nerves, reflexes, and objective sensory reactions normal. Blood and cerebrospinal fluid normal.

Discussion.— Dr. YEALLAND drew a diagram showing the anatomical relationship between the left striato-rubral pathway and both superior cerebellar peduncles, and said that he regarded the clinical features of this case as being consistent with a single lesion in the region of the left red nucleus. The patient described the pain as "shooting", and demonstrated its nature by thrusting his left index finger in several jerks downward from behind the right wrist towards his thumb, index and middle fingers. He (Dr. Yealland) regarded the distribution as well as the character of the pain as consistent with a lesion in the posterior nerve roots rather than with arthrogenous pain. Moreover, he thought that the wasting over 8C and 1D corresponded anatomically with the root level of the pain distribution, viz. 6C and 7C, because in view of Lissauer's tract the sensory root neurons ascended, before terminating, to a higher segmental level, the corresponding motor neurons leaving the cord two segments below. Could such a lesion be connected with the central lesion in this case? Would it be fantastic to suggest the possibility of a neurotropic virus, being cultivated in a long-standing arthritic joint, proceeding from the posterior nerve roots to the ventral horn cells. Could such a virus extend by way of the cerebellar tracts in the cord to the cerebellum, and thence to the superior cerebellar peduncles and the left pallidal system?

The PRESIDENT asked if there was X-ray evidence of arthritis of the cervical vertebræ.

Dr. YEALLAND (in reply) said that there was some evidence of arthritis in the shoulder and wrists only.

The PRESIDENT said that the tremor combined with the ataxy would probably be connected with a lesion involving the superior cerebellar peduncles. It was known that a tremor of that type could be associated with lesions of the red nucleus. Was there any cardiovascular disease? ("No.") The pain was, he thought, due to the arthritis.

Dr. MACDONALD CRITCHLEY said the clinical features recalled Lhermitte and Lejonne's description of "olivo-rubro-cerebellar atrophy", but knowledge of this affection was really confined to the one original case. He thought, as the President did, that the wasting and the pains were arthritic, and were outside the neurological picture.

Dr. WORSTER-DROUGHT said he considered that this case fell into the group of "delayed cerebellar atrophies". There were several variants or sub-varieties, including "olivo-rubro-cerebellar atrophy" and "olivo-ponto-cerebellar atrophy". The olivo-ponto-cerebellar form appeared to differ only from the more usual delayed cerebellar atrophy in showing an extensor plantar reflex.

Friedreich's Ataxy.—LEWIS R. YEALLAND, M.D.

Male, aged 15. Has always been clumsy in his gait; can now walk only with support. The disease cannot be traced in his relatives.

Physical examination.—Cerebellar signs: Nystagmus, and ataxy of arms and legs. Pyramidal signs: Double plantar reflex extensor. Lower reflex arc: Lost knee- and ankle-jerks on both sides. Deformity: Pes cavus. There is no loss of either postural or pain sense and there is no wasting.

Discussion.—Dr. YEALLAND said that he considered the functions of the patient's posterior columns to be normal. He had never before seen a case of Friedreich's ataxy which did not present some evidence of disease in those columns. Moreover, there was no reason to believe that there was any disturbance of function either in the posterior nerve roots or the ventral horn cells. Yet the deep reflexes in the lower limbs were absent. The loss of the deep reflexes in Friedreich's ataxy was often attributed, he thought wrongly, to disease in the posterior columns. It was common knowledge that Clarke's columns of cells were degenerated in this disease and that there was also an increase of neuroglia in the grey matter of the cord in that region. He was, therefore, of the opinion that the loss of deep reflexes in Friedreich's ataxy was due to a lesion in the connector neurons of the reflex arc in the grey matter of the cord. He did not think that any part of the arc of neurons concerned with the deep reflexes entered the posterior columns of the cord, but that the afferent limb ran straight into the posterior horns.

The PRESIDENT said that he had seen many cases of Friedreich's ataxy, particularly in his work at an orthopædic hospital, and it was not uncommon to find patients with lost knee- and ankle-jerks but with no demonstrable loss of sensation at all; that usually came a great deal later than the loss of the reflexes. He would not let it weigh against the diagnosis of an early case.

Acromegaly.—LEWIS R. YEALLAND, M.D.

Male, aged 28. Eight years' history of failing vision, bitemporal headache, general weakness, and changes in appearance.

Physical examination.—Typical acromegaly (fig. 1, p. 14). Discs: Double optic atrophy. Vision: Left eye is blind; right eye (acuity $\frac{6}{60}$) retains sight only in a reduced nasal field including central vision. Pupils: Left is inactive to direct but active to consensual light; right is active to direct but inactive to consensual light.

There are no other organic signs. Wassermann reaction negative in blood and fluid. The latter shows protein 0·16% and globulins in excess. A skiagram of the skull is consistent with an adenoma of the pituitary (fig. 2).

FIG. 1.

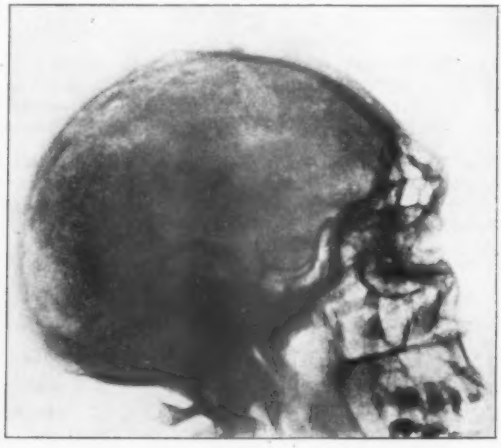

FIG. 2.

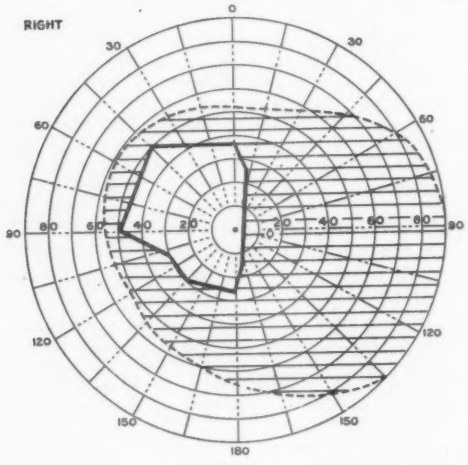

FIG. 3.

Discussion.—Dr. YEALLAND said that his reason for showing this case was not because it presented acromegaly almost in caricature, but because he regarded the behaviour of the patient's pupils to light to be of some physiological significance. Judged by the fields of vision (fig. 3) his sight was retained in the central field of the right eye, the acuity of vision of which was only $\frac{6}{60}$. Yet, when a light was thrown on the right retina, both pupils contracted normally to it. It might reasonably be assumed, he thought, from the visual fields that only those neurons which arose in and on the temporal side of the macular region

remained intact, the neurons arising from the nasal halves of both retinæ and from the temporal half of the left retina having perished by the pressure of the growth on the chiasma. The neurons which remained intact in this case included those which were commonly affected in disseminated sclerosis by retrobulbar neuritis, and in that condition the direct light reflex was lost on the affected side. Moreover, in many cases of retrobulbar neuritis, when the direct reflex to light was lost, the neurons arising from the nasal half of the affected side remained fairly intact, the loss of vision being represented by a central scotoma, somewhat the reverse of the features displayed in this case. He, therefore, thought that this case, when considered in conjunction with retrobulbar neuritis, supported a view that the neurons arising from the nasal halves of the retinæ did not participate in the transmission of impulses concerned in the light reflex.

Two Cases of Leaking Congenital Intracranial Aneurysm. Ligature of Internal Carotid Artery.—T. ROWLAND HILL, M.D.

I.—F. L., male, aged 29.

Three and a half years ago this man had a very severe attack of pain, of a thumping nature, on the top of the head. The pain continued intermittently for fourteen days.

Eleven months ago he had another, and more severe, attack of similar headache lasting three weeks.

Four months ago he was awakened from sleep by the noise of a street accident. He jumped out of bed and ran 500 yards from the house. He then experienced sudden severe pain over the left side of the forehead. With difficulty he returned to the house. He then vomited frequently for one hour, when he lost consciousness; he woke up again twenty-two hours later. On waking he still felt a severe pain in the left supra-orbital region, and vomited every few minutes. For a further fortnight the supra-orbital pains continued in paroxysmal manner and were followed by one week's freedom from symptoms.

At the end of the week he woke up to find his left eye half-closed, and he saw double. During the next twenty-four hours the eye closed completely. A day later there was a recurrence of "terrific" left supra-orbital pain. He became semiconscious and was admitted to hospital.

Thorotrast X-ray examination (fig. 1, p. 16) revealed an aneurysm of the left internal carotid artery and this vessel was ligatured. After operation pain was much relieved for two days, and then disappeared and has not recurred.

Just recently the patient has noticed the return of slight ability to open the left eye.

A left 3rd-nerve palsy is evident on examination, but there is no sensory loss in the 5th-nerve distribution, and there are no other neurological signs.

Lumbar puncture on admission showed the cerebrospinal fluid to be under normal pressure, but to be uniformly blood-stained, with xanthochromia on standing.

II.—A. F., female, aged 38.

Eighteen months ago whilst sitting down to have tea, after some active housework, the patient felt sudden severe pain at the back of the left eye. She felt "awful". "Like sinking down a deep hole." No loss of consciousness occurred. She went upstairs and lay on her bed, and was later able to walk to her doctor's house and back again. There was no headache until a few days later when this symptom appeared very severely over the vertex and was practically constant.

Eight days later the left eye gradually closed (taking forty-eight hours to do so). Freedom from headache followed for a few days, then there was a severe recurrence of pain (which seemed to follow a lumbar puncture) and which was in the distribution of the 1st and 2nd divisions of the left 5th nerve.

In July 1936 she was admitted to hospital.

Thorotrast X-ray examination revealed an aneurysm which seemed to be at the termination of the internal carotid artery, on the left side. Ligature of this vessel was afterwards carried out (figs. 2 and 3, p. 17).

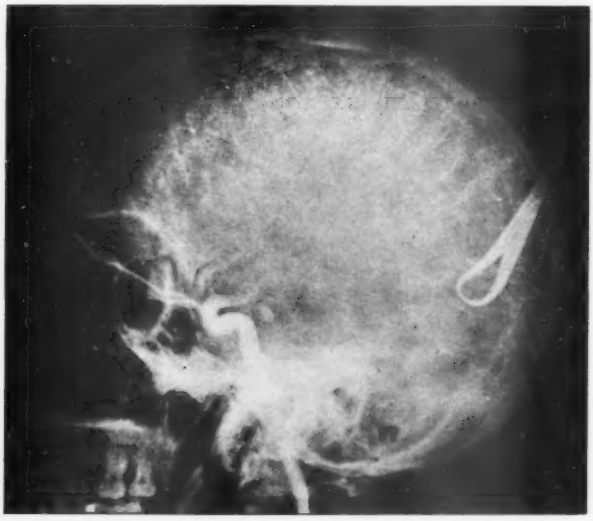

FIG. 1.—Thorotrast skiagram, showing an aneurysm posterior to the carotid siphon.

After a few days there was a marked diminution in the severity of the trigeminal pain, and on discharge from hospital one month later there was no pain at all. Six months later some power to open the left eye appeared, and improvement continued for three months.

The patient's condition has since remained stationary.

Discussion.—Dr. ROWLAND HILL described a third case of leaking intracranial aneurysm in which a thorotrast X-ray examination (fig. 4, p. 18) revealed the lesion. The patient was a woman aged over 70 and the history was remarkable. First, there had been a sudden attack of pain in the left supra-orbital region, and paralysis of the left 3rd nerve had occurred. This had rapidly cleared up, only to be followed a few weeks later by the rapid appearance of pulsating exophthalmos on the right side. This exophthalmos disappeared after six weeks, leaving a residual 6th-nerve paralysis. From the outset of the patient's troubles a systolic bruit inside the skull had been evident to her, and could be heard with a stethoscope on the skull. The bruit had persisted and about one year after the pulsating exophthalmos had cleared up there had been a sudden recurrence of pain followed by anæsthesia in the first division of the left 5th nerve and a complete left ophthalmoplegia. The bruit had simultaneously disappeared.

Thorotrast X-ray examination had revealed a large aneurysm at the termination of the left internal carotid artery. The vessel was ligatured and the patient had almost completely recovered and remained quite well. Presumably the systolic bruit had been due to an arteriovenous communication.

Dr. H. G. GARLAND said there seemed to be no doubt about the value of the procedure adopted in this case in saving the life of patients, but there was another aspect of the procedure, namely, the question of the development of hemiplegia, and, in the left-sided cases, aphasia as well. Was it possible to anticipate such complications? He had at the present time a patient who had been operated upon at that hospital—a fairly young man, who was aphasic, with severe right hemiplegia a year after the operation.

Professor P. C. CLOAKE asked whether the ligation of the carotid was done in one stage, or whether a cuff was put on the artery to compress it, as the initial operation was undertaken. When that was done there was, he thought, less risk of the patient developing

FIG. 2.—Thorotrast can be seen in the internal carotid artery and in an aneurysm posterior to this.

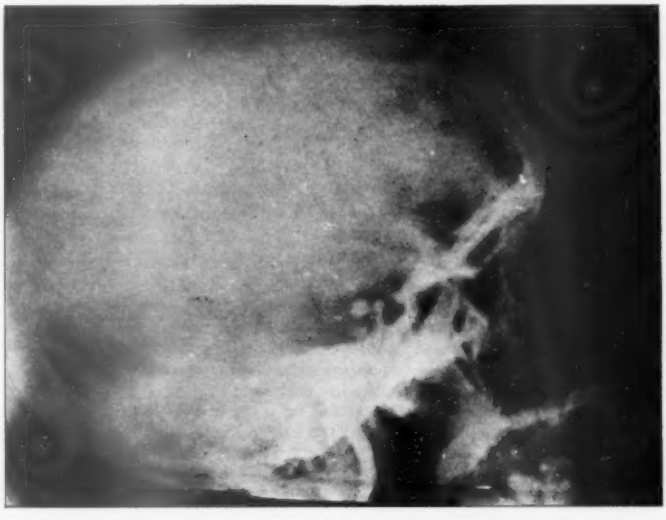

FIG. 3.—An exposure made a moment later. Some thorotrast has left the cavity of the aneurysm.

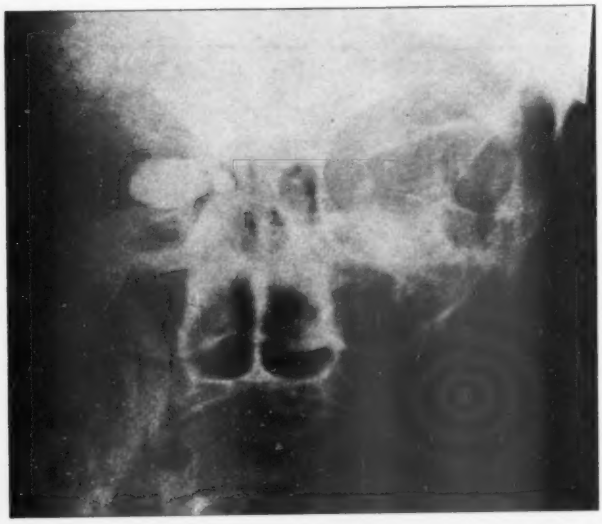

FIG. 4.—Thorotrast skiagram revealing a huge aneurysm at the termination of the left internal carotid artery in a woman of 70.

hemiplegia later on. He well remembered a case of the type which had been demonstrated, that was to say, severe pain over one eye had developed, with a 3rd-nerve palsy. Lumbar puncture had shown no blood present in the cerebrospinal fluid. Next day the patient had been leaning out of bed to reach his locker when the aneurysm burst, and he became unconscious and died. The post-mortem picture was interesting in that the 3rd nerve was lying on the body of the aneurysm. The original paralysis had been due, not necessarily to a leak, but possibly to a preliminary stretching of the aneurysmal wall.

Dr. ROWLAND HILL said that an American writer had dealt with the point which Professor Cloake had raised, and had concluded that the cavernous sinus syndrome was often due to what was called a "false" aneurysm. By that was meant a much enlarged sac produced by slight leakage and subsequent clotting.

Dr. DENNY-BROWN said that in the skiagrams of the first two cases the aneurysm lay behind the sinus, not in it, and therefore appeared to him to lie probably on the junction of the posterior communicating artery.

Dr. ROWLAND HILL (in reply) said that in the last case the bruit had completely disappeared at once, so that presumably there had occurred a squashing flat of the arteriovenous aneurysm. A case had been published of a bruit audible on the right side and pulsating exophthalmos on that side, due to an aneurysm which was shown, post mortem, to be on the left. In his case, because of the complete disappearance of symptoms and the patient's age, he had not used thorotrast on the other side. He was sure that in many cases the internal carotid aneurysms were outside the cavernous sinus, and that was why 6th-nerve palsy was often absent. It had been suggested that in about 25% of cases there was an aberrant circle of Willis, and that it was in this proportion that hemiplegia was likely to occur. But someone had concluded that if the internal carotid artery were occluded for thirty seconds, in most cases in which hemiplegia was going to develop there would be signs of it during that period. Therefore in all these cases the surgeon was asked to keep a clamp on the artery for several minutes before ligaturing. If then, after several minutes, no hemiplegia occurred, he proceeded with the operation, which was carried out in one stage.

The report of other cases shown at this meeting will be published in the next issue of the PROCEEDINGS *of the Section.*

Section of Laryngology

President—C. A. Scott Ridout, M.S.

[*November* 5, 1937]

Chronic Unilateral Ulceration of the Uvula Associated with a Nodule in the Mid-line of the Floor of the Mouth.—Herbert Tilley.

A surgeon, aged 53, consulted me on June 15, 1937, about a "chronic sore throat" which recently had been accompanied by pain on swallowing. He was sure that at no time had he suffered from any constitutional infection. The right side of the uvula was irregularly ulcerated and posterior rhinoscopy revealed a prominent bunch of granulations continuous with those seen at the base of the uvula. Palpation of the lesion gave a slight feeling of induration, but it was difficult to note any lack of mobility in the corresponding side of the soft palate. At the junction of frenum linguæ with the floor of the mouth there was a small, smooth, discrete, and freely movable nodule about $\frac{1}{10}$ in. in diameter. No enlarged glands could be detected in the neck.

Pathologist's report (Dr. W. W. Woods): Papillary growth from uvula, containing numerous atypical epithelial cells. Probably precancerous. No definite evidence of infiltrating carcinoma.

Radiotherapeutist's report (Dr. Roy Ward): He was treated on July 12 of this year by the insertion of radon seeds. Each radon seed had an activity of 1·5 mc. and was screened through 0·5 mm. of platinum. 17 seeds were used in the palate, 13 of which were fitted with threads and 4 unthreaded. The unthreaded seeds were implanted permanently, 2 seeds into the lateral pharyngeal wall on either side. The 13 threaded seeds were implanted in two semicircular rows, the distance between each row being 1·5 cm. and the distance between each seed being approximately the same. Five seeds, with threads, were inserted around the indurated area along the floor of the mouth on the right side between the mid-line and the position of the first molar tooth. All the seeds with threads were removed at the end of 168 hours.

Possibly the nodule would not have attracted my attention had I not seen an exactly similar one which developed about two years after I had removed (by diathermy) a primary epithelioma of the uvula. The nodule was dealt with by the same method, and there were no signs of its recurrence last July.

Discussion.—H. Bell Tawse asked what importance Mr. Tilley attached to the enlargement of the right submaxillary salivary gland.

H. Tilley said that he was inclined to regard the condition as inflammatory because in a similar case there had also been an enlarged left submaxillary gland which had taken many months to subside after extraction of a septic lower molar and removal of its infected root sockets.

Prolapse of Both Ventricles of Morgagni.—J. C. HOGG.

Male, aged 36, a plater in the Gas Light & Coke Co. Attended hospital on 12.10.37, complaining of hoarseness for two months. No previous history of throat trouble. Has done much singing; used to sing in public until about seven years ago. General health very good. On laryngoscopy a large polypoid swelling is seen emerging from the right laryngeal ventricle. A similar, but smaller, tumour is present on the left side. Examination of nose and fauces negative. No tubercle bacilli in sputum. Skiagram of chest normal. Wassermann reaction negative.

Discussion.—F. C. ORMEROD asked whether Mr. Hogg had examined this patient with a laryngeal probe. A prolapse of the ventricle was easily returned into position on pressing it with a probe. Dr. Irwin Moore, in association with the late Professor Shattock, fifteen years ago, collected all the cases of the kind which had at that date been reported, 85 in number. Their opinion was that the majority were inflammatory, and not true cases of prolapses. At a chest hospital a number which were of tuberculous nature were encountered and the swollen membrane could not be returned by pressure. This was of value as a diagnostic sign.

E. D. D. DAVIS asked whether Members had noticed a prolapse on the other side also, namely, a swelling far forward. It appeared to him to be like an inflammatory œdema of the ventricle on the right side, and possibly also on the left. Perhaps Mr. Hogg would examine the patient with the direct laryngoscope.

J. C. HOGG (in reply) said he had not attempted to push back this swelling into the ventricle. His impression was that there would not be an easy return, as the swelling was polypoid. He agreed there was a swelling on the other side too; this was probably an early stage of the same condition.

Tumour of Tongue : Thyroid.—MYLES L. FORMBY.

Female, aged 13 years. Swelling at back of tongue first noticed one year ago after tonsillectomy, gradually increasing in size, slightly painful. A flat papillomatous tumour, oval in shape, $1\frac{1}{2}$ by $\frac{3}{4}$ in., situated over the foramen cæcum, the central portion of the swelling is bluish in colour and covered with thick white epithelium.

A further history has been obtained from her father. She has had the swelling on the tongue four years. Two years ago the tumour became more evident, and it is thought that a piece was removed for examination. She has recently been pregnant, and her child was born five months ago; and the father is sure that during the pregnancy the tumour was much larger. During the last four months it has been subsiding.

Discussion.—HAROLD KISCH said that the thyroid was palpable in the neck, and that rendered the diagnosis of a lingual thyroid unlikely. He thought the appearance of the tumour itself was more suggestive of a papilloma.

WALTER HOWARTH said he did not agree with the idea that because there was a thyroid in the neck the patient could not have an aberrant thyroid in the region of the foramen cæcum. He had shown two or three cases in which there had been an aberrant thyroid in the tongue, and also a thyroid in the neck. He had removed the aberrant tumour, and there were no unfortunate symptoms.

Cicatricial Stenosis of the Larynx following Sarcoma of the Trachea treated by Radium.—E. WATSON-WILLIAMS.

A. O., female, now 12 years old.

History.—In 1931 patient had a sarcoma of the trachea (*Proc. Roy. Soc. Med.*, 24, 1637, Sect. Laryng. 125).

The subsequent history is as follows :—

September 1932 : Complete stenosis of larynx at level of cords.

May 1933 : Adhesion between cords divided : catheter sewn in for ten days. Sounds passed from tracheotomy wound after removal of catheter.

November 1934 : The cords remained separated, except at the anterior commissure. From this region a nodular mass of fibrous tissue was removed. Since then the child passes a bougie upward daily. A T-shaped tracheotomy tube was used to help in directing the air-current upward, but it was not possible to abandon the use of a tube ; little but scar tissue remains to represent the upper two rings of the trachea.

November 1937 : Mother reports, " General health excellent, her most serious ailment being a rare slight cold (when the tube gives some trouble). She cycles two miles to school daily, plays tennis and hockey, and is in the school gymnastic display team. Her father died in the spring of this year from a growth which developed suddenly in the lung. He was only ill for a week. The voice is a loud whisper ".

Laryngeal Carcinoma.—E. WATSON-WILLIAMS.

Mrs. E., aged 35.

History.—Diphtheria at age of 12. Married six months ago. October 1937 : Complains of hoarseness, during one year, without any pain. In the course of a month voice reduced to a hoarse whisper. No dysphagia ; no loss of weight noticed. Slight cough ; no sputum ; a little dyspnœa on exertion.

On examination.—The whole of the left vocal cord is replaced or hidden by a cauliflower mass reaching to the mid-line, the inner face apparently ulcerated. The arytenoid region and ary-epiglottic fold are thickened and quite fixed, but without œdema. The right half of the larynx—including inter-arytenoid region—is quite normal. Wassermann reaction negative. Repeated tests of sputum are negative for tubercle bacilli. No physical signs in the chest. Radiological report : " Old healed phthisis with calcification ; no active lesion seen ".

Report on biopsy : " Squamous carcinoma, Type II."

F. C. ORMEROD agreed that the section was one of squamous-celled carcinoma, with cell nests. A similar case, in which he had assisted Sir James Dundas-Grant, was that of a woman aged 29, who had been thought tuberculous. Her larynx was removed fourteen years ago, and she was still without any recurrence. No surgery short of complete removal of the larynx would cure the patient in the present case ; as she refused operation, treatment by the radium bomb might be tried.

Vasomotor Rhinitis

By E. SCHMIEGELOW (Copenhagen)

EVER since my earliest days as a rhinologist I have been greatly interested in vasomotor rhinitis. In 1883 I visited Wilhelm Hack, at Freiburg, shortly after (*Wien. med. Woch.*, 1882 and 1883) he had called attention to the phenomenon that certain parts of the nose might form the starting-point for a number of different neuroses which might be cured by a radical operative treatment of nasal affections. During my stay at Freiburg, Hack was very eager to develop his theories concerning the origin of these nasal reflex neuroses, and in his clinic which was crowded with patients from all corners of Europe, I had the opportunity of seeing a number of striking and characteristic instances of these reflex lesions which yielded, apparently, at any rate, to the treatment given by Hack. In the following year, 1884, Hack published his famous work : " On operative radical treatment of certain forms of migraine, asthma, hay-fever, and numerous kindred phenomena ". This work

attracted great attention, not only among rhinologists, but also among the medical profession in general, and contributed greatly to raise the estimation in which rhinology was previously held by physicians in general.

I shall not here enter into the wealth of personal and literary observations that make this book of Hack such interesting reading but will merely state that he attributed vasomotor coryza and hay-fever to irritation of the erectile tissue of the nose, and considered that it might be cured by operative removal of this erectile tissue—in particular that located on the anterior end of the inferior turbinated bones.

It was soon realized, however, that Hack was going too far when he looked upon all forms of neurosis as nasal reflexes, for in this category he included not only vasomotor rhinitis and hay-fever, but also many affections such as migraine, asthenopia, and other conditions. In the same year as his book was published, Hack's theories were the subject of a critical review by Bernhard Fränckel who read a paper (" Reflex Neuroses Originating from the Nasal Cavity ") before the Laryngological Section of the International Congress of Medicine at Copenhagen, 1884. In the discussion following this lecture, some of the prominent laryngologists of that time said that the views of Hack were true on several points, but that they were exaggerated, and that neuroses could be elicited from other parts of the nose besides the anterior end of the inferior turbinates; furthermore, it was claimed that galvano-cautery treatment was often abused in rhinology, because many physicians employed it indiscriminately.

I have mentioned these theories of Hack, which are now over fifty years old, because to my regret I have noticed that recent works on hay-fever, vasomotor rhinitis, and kindred conditions, fail to mention the authors of those early days, although their views laid at that time the foundation for subsequent research in vasomotor rhinitis and similar pathological conditions. It was Hack and other authors in the following decades who originated a later methodical research in the pathogenesis of these affections, but the results of this later research have been rather negative when we consider the enormous amount of time and work that have been devoted to this question.

Vasomotor rhinitis is subject to great variations in the intensity with which it manifests itself, ranging from a few brief and periodical attacks of convulsive sneezing to continuous attacks lasting all day long or more. In a case described by Mosler (*Virchow's Archiv*, **5**, 14; cited from Hack, l.c., p. 77) the patient, a woman, sneezed no less than 48,000 times within a period of eighty hours.

It has later been ascertained that vasomotor rhinitis is not due to an affection of the anterior end of the inferior turbinates, and that the disease, with its typical attacks of convulsive sneezing followed by watery secretion and congestion of the nostrils, which often sets in after awakening in the morning, is as a rule to be considered an allergic affection. But even though it may be reasonable to ascribe the disease to allergic substances, the problem is by no means solved, looked upon from the standpoint of the patient, if we do not know the particular allergic substance or the physiology of the nasal vasomotors.

Notwithstanding the work that has been done in this field, the physiology of the nasal vasomotors is still far from clear. Thus, there is a great divergence of opinion as to the innervation of the blood-vessels of the nasal mucosa. Some investigators deny the sympathetic nervous system any significance whatever in the vascular innervation of the nasal cavities, while others hold that it has a vasoconstrictor action, and a few assign to it a vasodilator action in the nasal cavity; finally, some investigators take its action to be constriction as well as dilatation of the blood-vessels in the mucous membrane of the nose. I here refer those who are interested in this question to a comprehensive work by W. Undritz, an assistant to Wojatschek of

Leningrad. In this work ("On the Vasomotor Reflexes of the Nose", *Zeits. f. Ohrenh.*, 1930, **25**, 157), Undritz gives an account of the experiments done so far in order to elucidate the innervation of the nasal mucosa.

Some investigators claim that the disease is due entirely to an affection of the superior cervical ganglion which keeps up an angiospastic condition of the nasal mucosa. As a result of this the mucous membrane is pale between the attacks, while its blood-vessels are swollen during the attack, owing to vascular paralysis. In such patients the nasal mucosa does not look pale in every case. Not infrequently we meet with patients in whom there are typical, daily recurring attacks of coryza and sneezing, and in whom the nasal mucosa still looks normal in thickness and colour.

We are still in want of a clear understanding of the physiological conditions underlying vasomotor rhinitis, nor can we identify the allergen that brings about the attacks. If we were able to identify the allergen we might also be able to protect the patient against the effect of the particular substance that elicits the attacks when it is introduced into the organism. Unfortunately, it is only in rare instances that we are able to demonstrate a specific allergen. In all probability the attacks are due to substances that are inhaled through the nose and exert their action directly upon the mucous membrane, such substances are not likely to produce specific skin reactions, and thus we lack the means for determination of the nature of the allergen.

It is justifiable to assume that the development of allergic vasomotor rhinitis requires two conditions: (1) A specific allergic substance that comes in contact with the nasal mucosa; (2) a particular character of the mucous membrane which is susceptible to the entrance of the allergic substance.

Most likely the allergic substances are always present, to a greater or less extent, in the atmosphere surrounding us—perhaps with the exception of seasonal periods in which some allergic substances disappear. It seems reasonable, then, to assume that hypersensitiveness of the nasal mucosa must be one of the principal conditions for the development and manifestation of such allergic attacks. If not, we would all be troubled with vasomotor rhinitis, periodically or continually.

This hypersensitiveness of the nasal mucosa may be congenital, for we meet frequently with patients who have suffered from vasomotor rhinitis all their life, even in childhood. On the other hand, this hypersensitiveness may also be acquired later in life, and in such cases the vasomotor rhinitis may be seen in otherwise normal robust adults in whom the nasal phenomena make their first appearance in direct connexion with an attack of influenza, coryza, pneumonia, tonsillitis, or similar acute infectious disease.

To Hack goes the credit for having shown that treatment of the nasal mucosa by galvano-cautery can in some cases check the vasomotor rhinitis, but he did not always succeed in this because he applied his treatment exclusively to the anterior end of the inferior turbinate, to which he believed the disease was localized. The results obtained with the galvano-cautery were better after this treatment was extended to include also a particularly hypersensitive zone on the septum of the nose, the so-called tuberculum septi. In earlier years I have obtained many excellent results in this way. Relapses are observed, however, even after this treatment—probably because the destruction of the mucous membrane is not extensive enough. In later years, therefore, I have tried another form of treatment in these severe relapsing cases of vasomotor rhinitis, and this method for extensive desensitization of the nasal mucosa has, in a great number of cases, yielded some particularly favourable results.

This treatment involves electrocoagulation of the nasal mucosa by means of a flat electrode. The patient having been narcotized, the blade-shaped electrode, which is insulated except at its point, about 1 cm. in length, is introduced in the nasal cavity between the inferior turbinated bones and the septum. The

current is closed, and a boiling hissing sound is heard, due to the coagulation and intense heating of the soft tissue, which is boiled in this way for about ten seconds. Then the current is turned off and the electrode is taken out.

I have now performed this operation in more than 50 cases, and have found that it causes neither pain nor general disturbance. Ethyl chloride is given and the patient is told to breathe deeply and slowly and count aloud the number of breaths. This makes it possible to watch the depth of the anæsthesia, as insensibility sets in when he ceases to count correctly. The administration of ethyl chloride is kept up for a few seconds more and then the mask is removed from the face. The patient is now ready for the endonasal electrocoagulation, and he does not feel the slightest pain during or after the operation. In spite of energetic electrocoagulation, none of the patients has ever complained of any pain afterwards, nor has there ever been any febrile reaction after, so that the operation may very well be performed on out-patients.

After the operation the mucous membrane presents whitish areas of coagulation necrosis, the extension and depth of which will depend upon the intensity and duration of the electrocoagulation. These membranous areas disappear slowly, in from two to four weeks. The operation should never be performed on both sides at the same time; after it has been performed on one side, it should not be done on the other until the first has completely healed.

Discussion.—HERBERT TILLEY: It has long been recognized that vasomotor rhinitis is an allergic manifestation and, as such, it resembles asthma, hay-fever, and some of the fugitive skin rashes. Furthermore, the allergen to which one patient is sensitive may be of an entirely different nature from that which affects another. Perhaps the symptoms of paroxysmal rhinitis and some clue to their treatment can be better envisaged if we bear in mind that whatever may be the allergic factor, this affects the autonomic, or involuntary nerve supply of nasal mucosa by way of sympathetic and parasympathetic fibres which pass through the Vidian nerve to the spheno-palatine ganglion. From thence they are re-laid to the nasal nasopharyngeal, palatal, and faucial regions (*see* Neil Maclay "Nasal Neuroses", *Brit. Med. Journ.*, 1924 (ii)). As one who, for many years, was a victim of asthma and associated vasomotor rhinitis, I have a vivid recollection of the needle-like pricking sensations in those areas, which always heralded the bronchial and nasal symptoms.

Obviously our first duty will be to discover the allergic factor of the nasal syndrome which may, or may not, be associated with asthma. Long-suffering patients of average intelligence can often give valuable hints as to whether the allergen is air-borne or enters the circulation by way of the gastro-intestinal tract.

A few instances have been recorded in which the stimulus proved to be of psychical origin and this is the more intelligible if we remember the effect of sudden fear or anxiety on the secretion of the suprarenal glands and their sympathetic innervation. When the source of the irritant cannot be traced by close questioning the patient, intradermal tests for the more common ones should not be neglected.

This seems to be an opportune moment for stating that infection of the nasal sinuses, or any other septic foci, seems rarely to be present, or ætiologically associated with vasomotor rhinitis.

Its nasal symptoms are more frequent in the female sex, and their prevalence has increased during the last five or six years since powdering the face has appeared to be necessary at daily decreasing intervals. "Orris root", which forms an element in some powders, has often proved to be the cause of the allergic nasal reactions.

It has often seemed impossible to identify the source of the paroxysms. In such circumstances I have seen much benefit and sometimes almost a cure following the administration of calcium lactate and parathyroid gland extract—a combination which is available in compressed form.

If, between the attacks, the swollen nasal mucosa is seen to be anæmic, the clear, thin discharge will generally prove to be alkaline to the litmus paper test. Internal medication by an acid mixture will then often cure the nasal symptoms and restore the membranes to their normal colour and consistence.

Highly sensitive areas or "spots" on the mucosa can frequently be detected by a blunt probe in chronic cases of vasomotor rhinitis. The more frequent are at the anterior end of inferior and middle turbinals and on the septum opposite the latter. Such regions should be treated, because even a draught of cold air or a dusty atmosphere will suffice to bring on an attack. It has been my practice to cocainize those regions, dry them, and apply a smear of trichloracetic acid, which is very penetrating and therefore more effective than superficial galvano-cauterization.

Bearing in mind that the nasal syndrome is a local manifestation of a sensitized sympathetic innervation, surgical procedures should be strictly limited to the removal of anatomical irregularities and pathological hypertrophies which narrow the upper air-ways.

JAMES ADAM said that there were at least three types of rhinitis. The first was milk rhinorrhœa; this was most common, especially among children. In many cases he (the speaker) had prohibited milk and the method had succeeded. His worst case had been that of a boy aged 10, whose upper lip had become raw owing to the constant streaming of watery fluid from his nose. Asked if the boy drank much milk, his parents had replied that "he would steal milk." He told them to stop the milk and bring him again in a fortnight. There had been no further trouble with him, except on the occasion of a Sunday-school trip, when, on the day following, his nose was again streaming.

The next kind of case seemed to be of the opposite type. The late Arthur Hutchinson had sent to him a patient, aged 50, whom he (Mr. Hutchinson) had been treating without benefit. After treatment by calcium gluconate there had been no more trouble. Thus in the latter case calcium was given, in the former it was withdrawn by forbidding the milk. He agreed with Mr. Tilley that there was a type of case in which calcium with vitamin D did good.

A third type was the aspirin-sensitive type. These patients had typical allergic symptoms, with excessive permeability of vessel walls, and their noses tended to stream and to form polypi. What occurred in that condition he did not know, but he thought they showed a strong tendency to acidosis. The patients in Mr. Tilley's cases mostly had achlorhydria. Sixty per cent. of his (the speaker's) own cases of asthma had defective gastric secretion, at least, as estimated by the fractional test.

R. SCOTT STEVENSON said he had found one or two rather slighting references recently to the method of treatment introduced by Alexander Francis some years ago. If used according to the method Francis advised, it frequently succeeded. After first searching with a probe in the nose, and especially on the septum, for sensitive spots, these were touched gently with a dull, cherry-red cautery; this was done on from three to five occasions. A considerable proportion of cases of vasomotor rhinitis could be improved by that simple method properly carried out; it was simpler and less harmful to the mucosa than ionization, a process which had been unduly boosted recently. He had used trichloracetic acid once or twice, but did not propose to do so again. On one occasion he put a touch of acid on each side of the nasal septum, where there was a sensitive spot, and next week there was quite a large perforation at that place. With regard to orris root, which had been mentioned, he had had an interesting case of vasomotor rhinitis, in an allergic patient. She was sent to Dr. G. W. Bray, who found that she reacted to orris root. She was advised to stop using her face powder, of a well-known make, and try something else, but the makers were insistent that no orris root was in it. It was then found that the patient was fond of white peppermint sweets, one of the constituents of which turned out to be orris root powder.

FRANK COKE said he did not think it was a difficult matter to discover antigens of an air-borne nature, such as dust or other proteins, to which the patient might be sensitized. Another potent cause of vasomotor rhinitis was the bacterial one. A swab should be taken from the post-natal space to see what organisms were present.

It was curious that the chief time for the sneezing attacks was first thing in the morning. Possibly when the patient awoke he stretched, and a large amount of foreign matter entered the blood-stream from the lymphatics thereby causing the sneezing.

H. V. FORSTER said he believed that the late Dr. Storm van Leuwen had emphasized the importance of animal emanations. Young girls employed as confectioners' assistants sometimes developed vasomotor rhinitis and this complaint might arise not so much from the

irritation of flour as from mites in flour. Van Leuwen had divided respiratory allergics into specific and non-specific groups and had found that the non-specific group reacted constantly to human dandruff. Many patients with vasomotor rhinitis were susceptible to cold and so were disturbed when getting up in the mornings; changes of temperature were perhaps the commonest cause of such reactions in susceptible individuals.

Dr. Adam had called attention to the possibility, in these days when milk was being distributed freely to school children, of many of them being sensitive to it, so that it might arouse vasomotor attacks in the nose, or even be a contributory cause of allergic deafness in young people. Vasomotor rhinitis was common in children and this should be taken into consideration when such children were sent as candidates for a tonsil, or tonsil-and-adenoid, operation under the schemes of the Education Authorities.

W. S. THACKER NEVILLE said he used ionization as a preventive of hay-fever, but if a patient already had hay-fever he did not do anything. This year he had used 1 c.c. of a 4% solution of histidine and the result was miraculous. The nose of the patient had been much obstructed but one injection had cured him; histidine, however, would not have much effect on chronic vasomotor rhinitis.

The Operative Treatment of Chronic Sinus Infection

By BEDFORD RUSSELL

THE purpose of this paper is to emphasize the *continuity* of chronic sinusitis, and also the importance of œdema and osteitis in the maintenance of the disease, and the diagnostic importance of œdema and hyperæmia as opposed to the presence of pus. Twenty-five years ago, if transillumination showed dullness of an antrum, it was lavaged. If pus was found sinusitis was diagnosed, and if no pus was found it was usual to ascribe the symptoms to *nerves*, the opacity being then ascribed to the sclerosis of past infection, but the sclerosis of the mucosa or bone was not always regarded as indicating any legacy of disease. Sinusitis was considered to be a thing of no continuity, though it was noticed that some people got more attacks than others. Experience of war wounds proved the persistence of residual sepsis in bone and other tissues, and with much careful histological work (Johnathan Wright and Smith[1] and Pickworth[2]) have paved the way for the recognition of sinusitis as progressive. Though the vast majority of nasal infections may resolve completely, many do not; anyone who suffered badly from the infections of the years 1890, 1918, 1929, and 1932 has probably retained histological evidence of them in the mucoperiosteum of his sinuses. The signs and symptoms of sinusitis in a given individual tend to alter with the passage of the years, and a patient who is suffering from sinus-headaches will say, "There is nothing wrong with my nose. I used to suffer dreadfully from colds, but now I never use a handkerchief and you can't give me a cold".

In the past an undue amount of attention was paid to the presence of pus as a diagnostic point, but I now regard imprisoned subepithelial œdema as the essential lesion in the maintenance of chronic sinusitis and in promoting its spread. Swelling of soft tissues in response to inflammation is either due to hyperæmia or to œdema. If the œdema is produced by blockage or increased permeability of the lymphatics, its pressure cannot rise above the blood-pressure; but the intrinsic œdema of the individual cells forming the submucous layer of the nasal mucosa is due to increased osmotic pressure caused by the breaking down of large colloidal molecules into small ones; this pressure can be higher than the blood-pressure, being the probable cause of the death of the mucous membrane occasionally seen in acute frontal sinusitis.

There is a fundamental difference between the mechanical conditions obtaining in the nose and those elsewhere in the body, in that among elastic tissues there is

[1] "Textbook of Diseases of the Nose and Throat", New York, 1914.
[2] "Chronic Nasal Sinusitis and its Relation to Mental Disorder," London, 1935.

room for œdema to come and go, whereas in the closed box constituted by the nasal cavities, and in particular by a sinus with a blocked ostium, œdema assumes an overwhelming mechanical importance. The rate and extent of the production of œdema, even in chronic conditions, are both surprising, and they were not easy to observe before the use of contrast-media in radiology. The films shown indicate that the mucosa can swell so as to occupy a sinus to the exclusion of air (figs. 1, 2, 3, and 4). The effect of the œdema, shown in fig. 2, is to block the ostium as effectually as would bone.

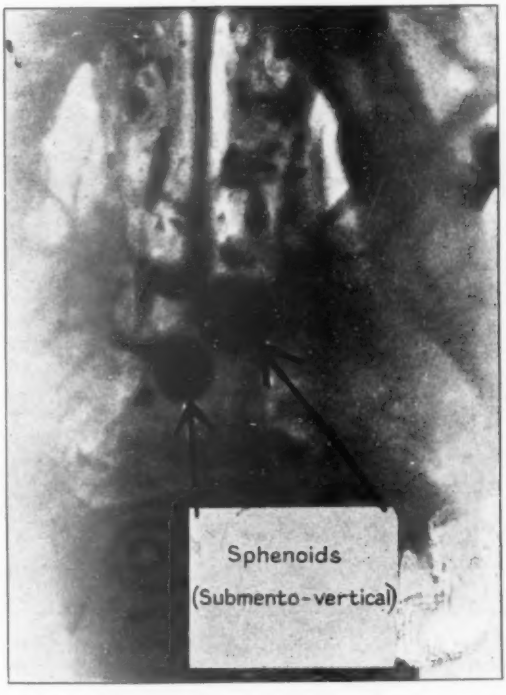

FIG. 1.—Taken on day of lipiodol replacement. No filling defect in sphenoids.

The ostium of a sphenoid which has been opened presents opportunities for observation not afforded by other sinuses, and I have seen an ostium close and open in a few seconds with subepithelial œdema.

Bone is permeable to fluids. We know (Sluder[3]) that cocaine will soak through the bony wall of a sphenoidal sinus and paralyse the Gasserian ganglion, and Ferris Smith found that the brain was stained by picric acid placed in a sphenoidal sinus denuded of its lining; also Pickworth's[4] work indicates that even organisms can go through from the sphenoidal sinus to the pituitary gland. It is to be expected

[3] "Some Anatomic and Clinical Relations of the Sphenoid Sinus to the Cavernous Sinus and the Fifth Nerve", *Trans. Amer. Laryng. Ass.*, 1912, **35**, 46.

[4] *Op. cit.* p. 8, footnote 2.

therefore that when pressure occurs in an infected sinus, the mucoperiosteum and finally the bony wall of the sinus become infected (Wright and Smith[5]). Lowndes Yates[6] showed that dyes were absorbed along the lymphatics from the sinuses with defective ciliary activity and quickly appeared in the urine ; when the cilia were active, the dye was swept out of the ostium, so that pus coming from an ostium may be indicative of a condition which is relatively healthier than one in which there is no discharge. Cases occur in which no pus appears in the nose, but in which the instillation of normal saline into the nose is followed by unmistakable signs of septic absorption. This possibility of toxic absorption from the nose can be rendered still more evident by Yates' test : If 0·4% indigo-carmine is sprayed into the nasal cavities

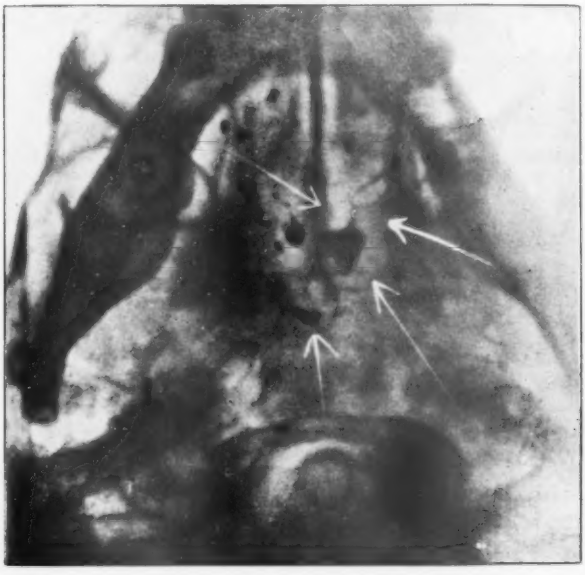

FIG. 2.—Vertical view. Fourth day after lipiodol replacement, showing swelling of sphenoidal mucosa with appearance suggesting partial obstruction to ostium of right sphenoid.

it is normally removed by the cilia and appears on the ciliary paths between the fauces. If toxic absorption is present, the dye appears in the lymphatics which run *beneath* the mucous membrane of the posterior pharyngeal wall. More striking still are the experiments of Le Gros Clarke upon normal guinea-pigs.[7]

One important point is the *duration* of the disease. A patient, aged 37, complains of one arresting symptom such as pain, for perhaps three months following an attack of influenza ; there is obvious chronic suppuration in the left antrum. The patient was born in 1900 and was well until he had a sore throat or bronchitis in 1918. This indicates a possibility of infection with the *Streptococcus pyogenes*. Inquiry reveals that pain over the left eye was a feature of the illness, but the oculist was unable to find any eye trouble. A skiagram shows not only an opaque left antrum but a

[5] *Op. cit.* p. 8, footnote 1.
[6] *J. Laryng. and Otol.*, 1924, **39**, 554.
[7] *Med. Res. Coun. Reports. Reports on Public Health and Medical Subjects*, 1929. No. 54, "Report to the Committee on Vaccination on an Anatomical Investigation into the Routes by which Infection may pass from the Nasal Cavities into the Brain."

slight haziness of the left frontal sinus as well. You cannot assure such a patient that an operation upon the left antrum will relieve the pain. If you drain the antrum only, and ignore the other cells which were once inflamed, you risk a post-operative aggravation in the frontal sinus followed by persistence of the pain.

It remains to decide in each case whether an isolated cell or group of cells is concerned, or whether the sinusitis has already become diffuse, and whether the œdema has become too advanced for simple drainage to cope with it. Failure to make such decisions justifies the derisive aphorism "Once a sinus operation, always a sinus operation!" We are often faced with a clear indication for an operation which may even be the fourth, although the earlier ones had been skilfully performed. It is to

FIG. 3.—Taken on day of lipiodol replacement. **Note suspension of the radiopaque upon swollen linings in antra.**

overcome this stigma that some surgeons have conceived operations which are condemned as too drastic.

The peculiar difficulties presented by the operative treatment of chronic frontal sinusitis have all been introduced by a laudable desire to avoid disfigurement. In the old days surgeons obliterated the sinus, and the disease, as a rule, was arrested. When sinusitis is confined to the frontal sinus I have employed Harmer's operation upon many occasions with satisfactory results: it has the advantage of being an ambulatory treatment.

The operation which Ferris Smith described here three years ago[3] is admirable in conception, technique, and results, so far as the sphenoidal sinus and ethmoids

[3] 1935, **28**, 963 (Sect. Laryng., 17)

are concerned, but it has limitations, imposed by the degree of osteitis. I have followed up nine cases since January 1935. In only two cases I have not been consulted since by the patient for more or less important symptoms. In two there has been pronounced discomfort with crusting and discharge. In one case diplopia persisted for twelve months. In the remaining four there has been continuous crusting and discharge, which has occasionally led to acute pain, owing to retention. Two have had to be re-opened, one for stenosis and one for trouble with the skin-graft. Skin occasionally gets out of hand when elevated above its station and used as a graft, the residual sepsis in the bone leads to a proliferative dermatitis which suggests cholesteatoma. The position of the incision is not quite the best. It is a curved

FIG. 4.—Lipiodol replacement three months later (palliative treatment). The radiopaque is now separated from antral floor by very slight degree of thickening of mucosa.

one, made upon a curved plane, so that contraction tends to make the scar stand out in a sort of web. I believe that a flat plane should be sought, and that there need be no fear of coming far forward in search of one.

In spite of these criticisms, the Ferris-Smith operation is a good one, and the patients are all grateful for the improvement.

If there were no osteitis, but only inflammation of the mucosa, there would be hope for a complete cure of any sinusitis by removal of the mucosa. But the underlying osteitis, no matter in which sinus, reinfects the new lining, whether that consists of columnar ciliated epithelium, scar-tissue, or squamous epithelium. In principle all infected linings should be removed where practicable, but limitations are imposed

by the osteitis, which sooner or later becomes a dominating feature in chronic infection in any sinus, and operation should be so planned that when the inevitable reinfection of the new lining occurs, the mechanical conditions will be such that sinus block cannot occur.

War experience taught the reality of residual sepsis, particularly in bone. The infecting organisms are encysted in a situation almost unassailable by the processes of repair. Luckily their power of resurrection seems to deteriorate with the years, but they are still there, and may take advantage of a new infection to leap into activity again.

Inflammatory activity in one septic focus is likely to be followed by activity in any or all other septic foci, and it is better to deal with the older focus first. It is easy to fall into the error of operating only upon that side on which there is pain, the original side having long since lost its power to put forth the remedial effort which may result in pain. Omission of the primary focus from the scope of the operation is likely to be followed by activity in secondary foci—such as infected kidneys—with serious results. I can recall such a patient in whom operations upon uterus, tonsils, and antra caused weeks of pyrexia, but in whom the opening of all the sinuses intranasally led to no pyrexia but to disappearance of symptoms which had not previously been ascribed to ethmoiditis.

If pressure develops in a focus, histamine-like juices are forced into the surrounding tissues, causing vasodilatation, so that refractory hæmorrhage should be an indication to speed up the operation rather than to spend the time trying to stop the bleeding. This vasodilatation is a guide in diagnosis too: if every part of the nose bleaches with adrenaline, except one middle turbinate, there is reason to suspect the presence of an infected and undrained cell somewhere under its shelter.

The operation described has been reserved mainly for the cases which have been operated upon several times previously, or in which a large operation was considered the only chance of improving them.

In 1934 Mr. J. B. Horgan came over from Cork to demonstrate how to reach the posterior sinuses and ethmoids via the antrum. I was so much impressed with the ease and safety of this approach and with the excellent exposure obtained that I have since employed a transantral approach in preference to an intranasal. Horgan is careful to leave the turbinates alone, and the interior of a nose treated by his method[9] shows little trace of operative interference, but while his method is ideal in cases of moderate duration in which osteitis has not become the dominating feature, I have been forced to reconsider the question of sparing the turbinates in severe cases in adults.

There is a natural reluctance to remove the inferior turbinate, and *if infected cells be left, removal is certainly followed by crusting*; but crusting is by no means inevitable. Crusting occurs in cases in which a skin-graft is used, and in all frontal-sinus cases which are grafted.

Skin-grafting may perhaps be employed in the fronto-nasal duct, but it should never be employed in the sphenoid, ethmoids, or antrum. Excellent immediate plastic results were obtained in many of these cases years ago, but in only one case in which the antrum was grafted has it been possible to leave it so permanently. The graft gradually becomes lifted up upon a layer of very tough scar-tissue which finally becomes œdematous, and upon the surface of it there form crusts which consist partly of squames and partly of dried secretion which has come from the neighbouring mucous surfaces.

The distress which results from the retention of secretion due to post-operative œdema justifies the operator in going to great lengths to avoid it. To the Horgan type of operation was added, first the removal of the middle turbinate, then that of the inferior turbinate, and finally the removal of the whole turbinate-bearing area. The

[9] 1926, *J. Laryng. and Otol.* **41**, 510.

nasal passage, ethmoid area, and antrum are turned into one large cavity and the procedure is termed " cavitation ".

After a suitable hypnotic, gas-and-oxygen anæsthesia is maintained through an intratracheal tube, to prevent blood gaining access to the larynx. A replacement is then carried out with adrenaline or neosynephrin, which diminishes the bleeding. The operation begins with a sublabial approach to the antrum, and usually includes a removal of the antral lining, but on occasion the antrum may be employed merely as a corridor for access to the posterior sinuses. The antrum is then packed with gauze soaked in peroxide while the anterior ends of inferior and middle turbinates are freed from their attachments.

The bony wall of the inferior meatus is next removed with a conchotome, after which a suitable flap is cut from the mucosa and allowed to fall over into the lower part of the antrum. The rest of the nasal wall of the antrum is then removed. An upward incision is made as far forward as possible, and meets the inferior turbinate

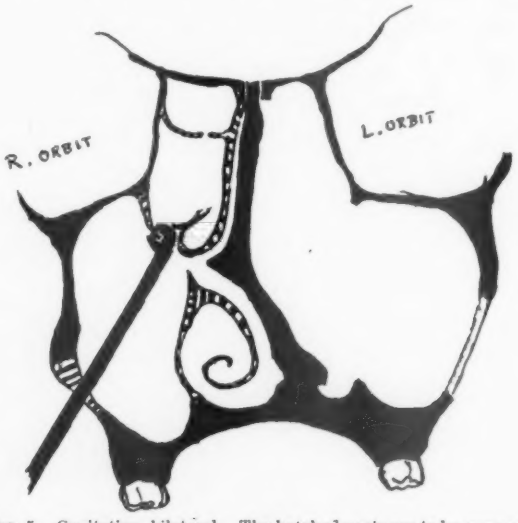

FIG. 5.—Cavitation, bilateral. The hatched parts are to be removed.

incision made through the nostril, freeing the turbinate and its supporting buttress anteriorly. The incision is continued up until it meets the floor of the anterior ethmoidal cells. The inferior turbinate is then swung outwards and is removed through the antrum. The antral wall where it forms the middle meatus, is removed with a conchotome.

The floor of the middle ethmoidal cells is next removed. The first step is the insertion of the upper blade of a sphenoidal forceps into the middle meatus through the antral ostium. The floor of this cell and then of all the anterior cells that can be reached is nibbled away till the wall of the orbit is reached, after which the posterior ethmoidal cells are treated in the same way.

The middle turbinate is then removed through the antrum, in the same way as was the inferior. In many cases it is now possible to remove the party-wall between the posterior ethmoidal cells and the sphenoidal sinus. An easier way is to find the sphenoid ostium intranasally, and remove some of its anterior wall, after which a

probe is left in the cell. This forms a guide with the help of which the spheno-ethmoid wall is removed with more confidence through the antrum.

The superior turbinate is next exposed by the removal of the intervening portions of the posterior ethmoidal cells. The larger blade of a large conchotome is placed in the olfactory cleft and the greater part of the turbinate is safely removed in one bite. Its remaining portions are then nibbled away with a small conchotome, and the removal of the nasal wall of the ethmoidal cell-mass is completed as far forward as possible. The mucosa is all removed, the bone of the anterior cranial fossa being left clean. In some cases it is possible to remove all the ethmoidal cells, and even part of the floor of the frontal sinus, which is desirable where feasible.

FIG. 6.—Cavitation operation. Left side.

During this part of the operation full use is made of the exposure permitted by the nasal combined with the transantral route. The nasal route alone is usually difficult and unsafe compared with the ease and safety afforded by the use of one route as a window through which the operator has visual control over instruments introduced by the other route.

The bleeding is often more than from a Caldwell-Luc operation, but just as in the antrum bleeding continues until the lining has been removed, bleeding from the rest of the cells continues until the operator has dealt with all the guilty cells. If there is doubt as to which cells need opening, it may be said that persistence of bleeding indicates that the task is unfinished. The arrest of bleeding thus obtained renders it unnecessary to pack the nose after operation.

When every attainable cell has been removed, the cavity is swabbed with strong

peroxide of hydrogen, which not only stops oozing but floats up small bony particles : and also, by the colour of the froth, indicates any small bleeding point which needs pinching. The sphenopalatine artery was ligatured on two occasions early in the series, but this has been found as unnecessary as it is in the case of the ethmoidal arteries. Reactionary hæmorrhage is rare.

After-treatment is confined for four days to the use of vasoconstricting sprays and the sniffing of coll. alk., after which discharge and crust are removed by suction, over a period of several weeks.

Pain, with swelling of the cheek, begins about the fourth day and is often severe for a week or more. In one bilateral case, apparently symmetrical, no pain occurred upon the first side, but pain was severe after operation on the second side three weeks

FIG. 7.—Cavitation operation. Left side.

later. Mr. Godsall, of the Prince Alfred Hospital in Sydney, tells me that pain is less in cases in which the periosteum is carefully sutured over the sublabial opening.

Otitis media is rare during the warmer months, but is not infrequent in cases which have perforce to be treated without a long interval after a cold.

Secondary hæmorrhage was common in the earlier cases in the series, but has been rare lately. This may be due to more nearly perfect removal of infected mucosa. It may also be due to the introduction of the use of prontosil ; the cases in which there is bleeding are always those infected with a hæmolytic streptococcus, and prontosil is given in any such case in which there is indication of post-operative infective activity.

If there has been radiological or other indication of the existence of frontal sinusitis

before the operation, latent sepsis in that cell may become active, and a logically planned operation in such cases should comprise external drainage of the frontal sinus either at the same sitting or later.

No case of meningitis has occurred, either with Horgan's operation or with this development of the operation that he described. One death only has occurred which was a direct result of the magnitude of the operation. The patient was having severe headaches in spite of palliative measures. All the sinuses were crammed with inflamed polypi which bled furiously, and the patient collapsed five hours after the operation. Two deaths occurred as the result of extending the sphenoidostomy till cancellous bone was reached. One of these patients, while at home five weeks after the operation, suddenly became ill. The skiagram showed absorption of the basi-sphenoid, and the patient died of osteomyelitis shortly afterwards. The third patient died of septicæmia. No post-mortem examination was obtainable, but I think that osteomyelitis probably occurred in this case also.

These three deaths were the only ones due to the operation, and give a mortality of under 2% during three and a half years, but I regard them as due rather to bad judgment than to the plan of the operation.

In each of these cases, the operation was performed for rapidly increasing headaches in cases of sinusitis of long standing.

Crusting does not seem to occur in the cases treated for asthma. Asthma is not sinusitis, although sinusitis may co-exist with the gross œdema which characterizes the sinus-lining of all the asthmatics I have seen. I do not consider that the nose of an asthmatic has been properly treated until all the sinuses which contain polypi have been widely opened, or better still relieved of their swollen linings.

In migraine also, although the pain in my opinion is generated mechanically in the sinuses, there need be no sinusitis, but the relief to the symptoms in two cases is convincing. The patients have had no migraine since the operation two years ago. In another case there was sinusitis, and the patient's chronic iritis was attributed to the condition of the left sphenoidal sinus. No pus was seen at any time in the nose, but the left antrum and sphenoidal sinus were full of polypi. She had a severe secondary hæmorrhage on the tenth day, probably due to a pre-existing hæmolytic streptococcal infection.

In yet another case giant urticaria began on the right side of the head and gradually spread to the trunk; no doubt it was derived from an antral infection due to old dental trouble. The ordinary skiagram showed no abnormality, but an œdema of the lining was clearly shown when a lipiodol replacement had been carried out.

Discussion.—A. J. WRIGHT said he thought that the way to avoid causing pain was to avoid bruising, and to avoid bruising a large incision should be made in the soft parts, so that the surgeon could work through an adequate opening, and remove bone with the gouge and mallet, rather than with a burr and punch forceps.

T. B. LAYTON said that he came intending to criticize Mr. Bedford Russell's operation, as it was the antithesis of all he was striving for in rhinology, namely, to devise and perform operations which removed the irreducible amount of mucous membrane, and, if possible, so left the nose that one could not recognize, with the nasal speculum, that any operation had been done. Yet he must admit that the patients shown by Mr. Bedford Russell had been materially benefited by the operation.

The important thing in the paper was the stress which was laid on the difference between suppurative sinusitis and the polypoid reaction unassociated with suppuration. He thought nobody should use the word "sinusitis" to-day without an explanatory adjective. In suppurative inflammation of the sinuses wonderful results were obtained from drainage operations, if properly performed. Such were of no use where there was nothing to drain, and he thought that was where many operations failed, because drainage had been continued for polypoid reactions.

The paper advocated the replacement of drainage by eradication, but he (the speaker) hoped that that idea would not last long. He believed that when the pathology of these

diseases had been studied more, non-operative means of treatment would be found, and that the secret of success would be in early and correct diagnosis.

G. EWART MARTIN asked what were the after-results of these cases in relation to crusting, and the effect on the nasopharynx and larynx. He had worked with Greenfield Sluder and was surprised to see that Mr. Bedford Russell removed the whole of the inferior turbinal and destroyed the inferior meatus. Sluder always insisted that if there was an antral, as well as an ethmoidal, infection, the antral drainage should be completed first and the ethmoidal operation performed later. In the radical antrum operation, in order to conserve the inferior turbinal and the inferior meatus, he always opened into the middle meatus instead of the inferior meatus, and removed the whole of the ethmoidal region as completely as Mr. Bedford Russell suggested. In Edinburgh they had carried out this operation for the last sixteen years with very good results, in spite of the criticism which was levelled against the operation as being too radical. Everyone, naturally, had fatalities in a radical ethmoidal operation, due to defects in the cribriform plate, which could not be foreseen and which might even complicate a septum operation. Free removal or destruction of the inferior turbinal was prejudicial to the condition of the pharynx and larynx, as the patient might develop a chronic laryngitis or a pachydermia, such as often followed atrophic rhinitis.

BEDFORD RUSSELL (in reply) agreed with Mr. Layton that there was probably an essential difference between streptococcal œdema and allergic œdema; he also agreed with Mr. Layton that the ideal treatment was non-operative. He had been brought up to regard operation as a confession of failure. Most of the patients under review had had a good deal of treatment of all sorts along conservative lines before he saw them. He had been struck by the number of these patients who said they would agree to have the operation over again, though it was painful, because of the relief brought to them which they had never gained under conservative measures. Colds should be treated with ephedrine; there would then be less chronic sinusitis to be treated surgically fifteen years later. Many people having had colds for ten years, then ceased to have them; and at 40 years of age they came with headaches, and said it was impossible to give them a cold. He thought the different complaints were merely manifestations of the same condition at different stages.

In reply to Mr. Ewart Martin, he was glad to hear from someone who had worked under Sluder. He agreed that the inferior turbinate must be regarded as a physiological body, but this operation was done for conditions which were ruining the patient's life.

Section of Obstetrics and Gynæcology

President—MILES PHILLIPS, M.D.

[*November* 19, 1937]

Maternity Work in L.C.C. Hospitals, 1931-1936

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THIS study of the obstetrical records of the maternity units in the London County Council hospitals is presented with all diffidence as a small contribution to the great problem of the reduction of the maternal death-rate. During the period under review there has been a 50% reduction in the rate in the Council's hospitals, i.e. from 7·98 to 3·51 (excluding abortions) and the general rate per 1,000 live births for London has fallen from 3·81 in 1931 to 1·98 in 1936. The conditions in municipal hospitals are in many respects different from those in the great teaching hospitals, but they are the conditions to which many of the students must adapt themselves after graduating, and they are the conditions under which an increasingly large percentage of the midwifery of the country is being conducted. 18,261 of the 58,130 births in London in 1936 took place in L.C.C. hospitals.

As a result of the Local Government Act, 1929, the London County Council found itself in charge of 600 maternity beds distributed among 22 general hospitals and 4 institutions. The size of the units varied from 12 to 52 beds and the standards of the equipment and accommodation were equally diverse.

Having regard to the high national rate of maternal mortality, the Council decided to make hospital admission available to all women without restriction. As soon as practicable the maternity units in Public Assistance Institutions were transferred to neighbouring hospitals, and active measures were taken to improve equipment accommodation and staffing of all units. Any estimate of results achieved should take into consideration the fact that this task has been a gigantic one and is still far from completed.

The development of the maternity department is summarized in Tables I and III, and the results in Table II. In regard to Table III (ante-natal clinics) it must be remembered that the Council has no power to make attendance at a clinic a condition of admission to the maternity wards, as is now customary at the voluntary hospitals. Nor have we any machinery for health propaganda under our direct control. The figures for ante-natal " bookings " therefore reflect the greatest credit on the health, education and intelligence of the women of London. The great majority of those recording one or two attendances at hospital clinics have also received supervision from a Borough Clinic or doctor or midwife. For the co-operation of the Borough Health services we owe a debt of gratitude.

Owing to the practical difficulties of collecting statistics from over 20 different units, the returns are not uniform over the period. Not until 1933 were the patients

divided into " booked " and " unbooked ", and only in the last two years have full returns of abnormal cases been made on the standardized forms.

TABLE I.—L.C.C. MATERNITY UNITS. 1931-36.

Year	No. of Units	Beds	Confinements	Births		Total	Ante-natal care at L.C.C. Clinic	Illegitimate rate	Primiparous rate
				Live	Still				
1931	26	600	10,038	9,696	495	10,191	No record	No record	No record
1932	26	646	11,239	10,974	451	11,425	No record	No record	No record
1933	24	666	11,668	11,414	503	11,917	83%	13·02%	44·1%
1934	24	723	13,050	12,738	515	13,253	87%	10·99%	44·89%
1935	23	783	15,280	14,915	604	15,519	89·5%	9·5%	45·4%
1936	22	853	17,926	17,563	698	18,261	90·88%	8·7%	46·5%

TABLE II.—L.C.C. MATERNITY UNITS, 1931-36. RATES FOR AIDED BIRTHS, STILLBIRTHS AND DEATHS WITHIN TEN DAYS.

Year	Total confinements	Aided or complicated		Stillbirths		Death within ten days		Cæsarean sections		Forceps		Surgical induction		Year
		No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	
1933	11,668	1,878	16·1	473	4·1	227	1·9	136	1·17	380	3·25	Not recorded		1933
1934	13,050	1,963	15·4	474	3·7	247	1·9	136	1·04	463	3·54	225	1·72	1934
1935	15,280	2,475	16·2	606	3·9	299	1·9	120	0·78	541	3·54	348	2·28	1935
1936	17,926	2,767	15·4	686	3·8	355	1·9	152	0·85	607	3·39	442	2·47	1936

TABLE III.—ANTE-NATAL SERVICES. 1931-36.

Year ended December 31	Total confinements	Ante-natal clinics		Percentage of cases that attended ante-natal clinics	No. of ante-natal clinic sessions held weekly	Post-natal clinics	
		No. of women seen	No. of attendances made			No. of mothers seen	No. of attendances made
1931	10,038	8,102	36,198	No record	33 sessions	No record	
1932	11,239	9,448	48,618	No record	39 sessions	Incomplete record	
1933	11,668	12,126	57,884	83%	54 sessions	3,352 (approx.)	5,205 (approx.)
1934	13,050	13,065	73,142	87%	—	4,078	6,013
1935	15,280	15,681	97,802	89·5%	74 sessions	5,015	7,542
1936	17,926	18,251	120,538	90·86%	101 sessions	6,140	7,867

MATERNAL DEATHS

The system of classification adopted in Tables IV, XIV, and XV demands an explanation. The main object was to present to the appropriate committee of the Council a fair picture of the efficiency of the obstetrical work in their wards. It was

TABLE IV.—MATERNAL DEATHS, [illegible] THE DEATHS [illegible] NANCY

Ante-natal care	1931			1932			1933		[illegible]
	L.C.C. clinic	Other or nil	Total	L.C.C. clinic	Other or nil	Total	L.C.C. clinic	Other or nil	[illegible]
Confinements	Not recorded		10,038	Not recorded		11,239	9,685	1,999	[illegible]
Causes of death :—									
Puerperal sepsis	12	8	20	8	4	12	10	8	
*Toxæmia: Eclampsia	1	3	4	2	10	12	1	5	
*Toxæmia: Pyelitis or nephritis	4	3	7	1	0	1	1	1	
*Toxæmia: Other forms	0	2	2	1	2	3	1	2	
Hæmorrhages: Accidental	0	0	0	0	3	3	0	3	
Hæmorrhages: Placenta prævia	3	3	6	1	2	3	2	2	
Hæmorrhages: P.P.H.	0	0	0	0	0	0	3	1	
Accidents of childbirth: Obstetric shock	2	4	6	2	1	3	1	2	
Accidents of childbirth: Rupture of uterus	1	0	1	2	2	4	1	1	
Accidents of childbirth: Pulmonary embolus	0	1	1	3	0	3	6	0	
Anæsthesia	1	3	4	0	0	0	2	0	
Puerperal insanity	0	0	0	0	0	0	1	0	
Miscellaneous	0	0	0	6	0	6	2	1	
Totals	24	27	51	26	24	50	31	26	

* Includes death[s] occ[urring] y perio[d]

therefore found necessary to adopt an individual method which showed the abortions separately and distinguished as clearly as possible between deaths due directly to pregnancy and labour, and those due to coincident disease. Any attempt to give figures comparable with the Registrar-General's statistics led to absurd results owing to the preponderance of abortions. A time limit of four weeks after confinement was adopted for the "associated" group, but for those directly due to the pregnancy or labour, no limit is made. The mortality rate for the deaths due to pregnancy and labour was 2·51 in 1936 and for associated deaths 1·00. For the women who had had ante-natal care at our own clinics the rates were 1·53 and 0·43.

Since 1934, all deaths in which permission for a post-mortem can be obtained are notified to the Central Pathological Laboratory, Archway Hospital, and the autopsy is conducted by or in the presence of Dr. Barnard or Dr. Bratton, who sends a full report to the Medical Officer. These routine reports by specialist pathologists are the commonplace of the teaching hospitals but are not so common in other circumstances. I would emphasize that we have found them invaluable, and it is suggested that they should be included as an essential part of any properly organized maternity service.

In 1936, permission for a post-mortem was obtained in 88% of the deaths, and in none of those in which it was refused was the diagnosis in doubt.

Puerperal sepsis (Table VI).—This still remains our major problem. The incidence of sepsis has, however, been assessed at the maximum. Mastitis, death from sepsis after Cæsarean section, many pulmonary emboli, cases of acute bacterial endocarditis, and septic pneumonia have been included. Where there was any doubt as to the original infection being uterine, sections were taken of the uterine walls and vessels.

Two factors have revolutionized the outlook in sepsis during the period under review, i.e. the intensive work of Dr. Colebrook and his colleagues on the hæmolytic streptococcus, and the discovery of prontosil. The former is an invaluable factor in prevention, the latter will be in treatment, but came too late to really influence this series. We have lost three patients only from hæmolytic streptococcus infection since the use of prontosil became general, and two of these were infected outside our wards. An intensive study from the bacteriological standpoint could add little to the work already done by others, but it may be worth while to present some comments on the general aspects, which are no less important.

Puerperal sepsis appears in hospitals in four main groups.

(1) As a result of pre-existing septic foci, e.g. foul vaginal discharge from lacerated

...THS, 19...ER THE 28TH WEEK OF PREGNANCY).
...ATHS ...NANCY OR LABOUR.

1933		1934		1935		1936			1931-36		
Other or nil		Other or nil	Total	L.C.C. clinic	Other or nil	Total	L.C.C. clinic	Other or nil	Total	L.C.C. clinic	Other or nil	Total
1,999	1	1,630	13,066	13,692	1,599	15,291	16,302	1,634	17,936	—	—	79,254
8		6	15	8	4	12	11	7	18	58	37	95
5		4	6	1	3	4	3	3	6	10	28	38
1		2	4	2	1	3	0	1	1	10	8	18
2		2	4	2	0	2	0	3	3	6	11	17
3		1	1	0	2	2	0	2	2	0	11	11
2		2	2	1	2	3	0	2	2	7	13	20
1		2	6	2	2	4	3	2	5	12	7	19
2		2	4	3	5	8	2	0	2	12	14	26
1		1	1	1	1	2	2	0	2	7	5	12
0		0	0	0	0	0	1	0	1	9	2	11
0		0	1	1	0	1	3	0	3	8	3	11
0		0	1	0	1	1	0	0	0	2	1	3
1		1	2	0	0	0	0	0	0	9	2	11
26		23	47	21	21	42	25	20	45	150	142	292

...ths occ... period of pregnancy.

TABLE V.—DEATHS AMONG 41,430 "BOOKED" CASES (AFTER THE 28TH WEEK) 1934-36.

Eclampsia	6
Other forms of toxæmia and pyelitis	8
Accidental hæmorrhage	0
Placenta prævia	1
Post-partum hæmorrhage	9
Obstetrical shock	7
Rupture of uterus	3
Anæsthetic	5
Pulmonary embolus	1
Unclassified	1
Sepsis	28
Total	69

TABLE VI.—DEATHS FROM PUERPERAL SEPSIS.

	1931		1932		1933		1934		1935		1936		1931-36	
Confinements	10,038		11,239		11,684		13,066		15,291		17,936		79,254	
Group 1: Labour conducted entirely in L.C.C. Hospital / *Group 2:* Labour conducted partially outside Hospital	1	2	1	2	1	2	1	2	1	2	1	2	1	2
Normal labour	6	2	1	0	5	0	4	0	6	0	0	1	22	3
After application of forceps	1	0	0	0	2	0	0	2	2	1	2	3	7	6
Other complicated or abnormal labour	2	5	5	1	5	4	1	3	0	3	9	3	22	19
Mastitis	1	0	2	0	1	0	0	0	0	0	0	0	4	0
Cæsarean section (including hysterotomy)	3	0	1	2	1	0	4	1	0	0	0	0	9	3
Totals	13	7	9	3	14	4	9	6	8	4	11	7	64	31
	20		12		18		15		12		18		95	
Rates per 1,000 confinements	2·0		1·06		1·54		1·14		0·78		1·00		1·19	

cervix, cloacal opening between vagina and rectum left from a previous confinement, septic teeth, &c. Of the direct influence of teeth on maternal morbidity one can find little evidence, but for nutritional reasons good dentistry in the ante-natal period is, of course, important. Undoubted auto-infection is in our experience rare.

(2) Epidemics, in which the hæmolytic streptococcus is almost invariably the organism at fault. We have had one major epidemic in 1932, in a newly opened unit, with three deaths and eighteen cases. Otherwise this cause of infection has contributed very little to our death-rate.

(3) Sporadic infection after normal labour. This is largely dependent on the midwives who in our wards conduct normal deliveries, and it is greatly to their credit that in two years (1936 and ten months of 1937) out of approximately 35,000 deliveries conducted wholly in the wards they have only lost one patient from this cause. Deaths in women who were long in labour with ruptured membranes before admission, and two deaths in women who had had gonorrhœa, were allocated to other groups.

(4) Sporadic infection after abnormal labour. This remains as our chief difficulty. It cannot be solved, as is sometimes suggested, by the simple method of leaving things to Nature and treating all cases as though they were normal. Non-intervention has its limits of usefulness and undue delay in interference actually adds to the risk of sepsis. The misuse of forceps certainly plays no part in our mortality figures. It will be noted that in few of our fatal cases (7 out of a total of 64 in six years), have forceps been used at all. In every instance there were urgent indications; in several the patient was unmistakably septic before forceps were applied. A large variety of organisms may be present, which greatly adds to the difficulty of prevention.

The invaluable contribution of bacteriology to the control of puerperal sepsis may have the unfortunate result that too-exclusive attention is devoted to the hunt for the offending organism (or even to one variety of organism), while practical dangers

are ignored. A parturient woman is a patient and not merely a recumbent culture medium. One has known fatal epidemics where the bacteriological reports were impeccable but everything else wrong. Some of the danger points which need incessant vigilance may be outlined as follows :—

(i) Poor technique in normal deliveries and in ward management. The great hospitals and famous training schools have their own inviolable traditions, but in smaller units with frequently changing staff dubious practices are apt to creep in. We suggest that each hospital should work out a scheme of practical methods which can be committed to paper, made the basis of the ward practice, and improved as experience suggests.

(ii) Overcrowding in lying-in wards and labour rooms. This is a danger to which municipal hospitals are peculiarly exposed, as they retain their Poor Law obligation to admit the necessitous. Moreover, other hospitals regard them as their natural resource in emergencies.

(iii) Lack of separate accommodation for " suspect " cases. This is a grave problem in the older units and is a common source of infection and starting point of epidemics. Even the " booked " patient who has attended the hospital ante-natal clinic may arrive in a dangerously infective condition, owing to nasal catarrh, sore throat, local sepsis due to late coitus or early rupture of membranes, or even a belated and desperate attempt to procure a miscarriage. All patients should be passed through a receiving room and properly examined before admission to the main unit.

(iv) Faulty handling of sepsis when it occurs. It is not always remembered that many students and pupil midwives do not see a case of sepsis, however mild, during training, and are completely misled when they first encounter one. Hence one finds—

(*a*) failure to recognize early sepsis as such. The first case in many epidemics has been labelled " influenza " or " cystitis ".

(*b*) failure to remove a pyrexial case out of a ward with sufficient promptitude.

(*c*) failure to segregate pyrexial patients properly and to ensure that there is no channel left for the contamination of clean patients. Some specialists even advise that the nursing staff should be housed separately.

(v) Allowing access of staff or visitors with hæmolytic streptococci in their throats. Our nursing and midwifery staffs are swabbed before taking up duty in the maternity wards, but we avoid routine swabbing as much as possible. There is much evidence that the results are misleading, and on balance it does more harm than good. The disorganization of staffing it causes is disastrous.

We have now worked out a scheme for regulating ward closure for sepsis, which has been circulated for guidance to all hospitals with maternity units. The responsibility for action rests, of course, with the clinician in charge of the ward. It cannot be settled on purely bacteriological and still less on " rule of thumb " lines. Probably the most important suggestion is that all pyrexias should be removed promptly from the ward and that all, whatever the apparent cause, should have a swab taken from the genital tract.

A word should be said of mastitis, which remains the most baffling of all forms of sepsis. It appears in almost epidemic form in some localities (not only in the Council's hospitals), and goes as mysteriously as it comes. In our experience it is independent of the routine technique used for the nipple, and is as liable to appear where no handling is allowed as where elaborate precautions are taken.

Toxæmias (Tables VII and VIII).—In this group are included all examples of renal disease, as it has proved difficult in practice to separate cases of acute toxæmia with albuminuria of recent origin from those whose kidneys had sustained some damage in a previous pregnancy or otherwise.

TABLE VII.—ECLAMPSIA I (INCLUDING PATIENTS DELIVERED BEFORE ADMISSION) 1931-36.

	L.C.C. Clinic		Other or nil		Total	
Year	Cases	Deaths	Cases	Deaths	Cases	Deaths
1931	11	1	22	4	33	5
1932	18	2	17	12	35	14
1933	10	1	25	5	35	6
1934	12	2	29	6	41	8
1935	8	1	29	4	37	5
1936	14	3	18	4	32	7
	73	10	140	35	213	45
Case mortality	13·7%		25·0%		21·1%	

TABLE VIII.—ECLAMPSIA II. ANALYSIS FOR YEARS 1934-36.

Total Confinements in L.C.C. Hospitals 46,293.

		Cases of eclampsia	Deaths
	Total in 1934-36	110	20
Ante-natal Care			
	L.C.C. Clinic	34	6
	Other or nil	76	14
Parity			
	Primipara	82	13
	Multipara	28	7
Onset of Fits			
	Before labour	42	8
	During labour	33	8
	After labour	35	4
Maturity at onset of Fits			
	Before 28th week	3	1
	Between 28th and 32nd week	19	5
	,, 32nd ,, 36th ,, ...	17	2
	,, 36th ,, 39th ,, ...	26	5
	At and after term	45	7
Albuminuria			
	Large amount	81	18
	A trace	21	0
	None at any time	8	2
	Trace on discharge	21	—
Blood-pressures (95 cases)	Between 115 and 140	17	1
	,, 140 ,, 190	54	12
	,, 190 ,, 284	24	2

Eclampsia stands out as the commonest form of death, after puerperal sepsis. In view of the fact that it is often dogmatically asserted to be a " preventable disease " it may be surprising to find that the Council's ante-natal clinic patients furnished 73 cases in six years with ten deaths. One can only endorse Whitridge Williams' dictum " Those who claim that eclampsia can always be prevented are either misinformed or careless in the use of words ".

For the past three years a detailed return of all eclampsia cases has been received; of 41,430 women confined in our wards during this period who had ante-natal care at our clinics, 34 developed eclampsia and six died. Three of these were fulmi ant cases, with no warning of impending disaster either in the urine or the blood-pressure. In two cases the patients themselves refused to co-operate, and in one only was it felt that greater vigilance might have been exercised. All the deaths were at different hospitals.

Eight deaths from other forms of toxæmia and renal disease occurred in this group during the same period. Four were due to acute nephritis or pyelonephritis, three to what is now called " pre-eclamptic toxæmia ", and one was a complicated case of diabetes with superadded renal symptoms. Death from chorea gravidarum, hyperemesis, and acute yellow atrophy did not occur in over 41,000 deliveries.

During the same period (1934–1936) we had, among 4,863 emergency admissions, 76 cases of eclampsia, with 14 deaths. Many of the patients who died were comatose on admission. Nine women succumbed to other forms of toxæmia and renal disease. Acute and chronic nephritis and pyelonephritis account for four, acute yellow atrophy one, chorea gravidarum and hyperemesis gravidarum for two each. In addition a markedly toxæmic element was present in at least eight other patients whose death was primarily attributable to hæmorrhage, obstetrical shock, puerperal mania, or sepsis.

The rarity of true hyperemesis gravidarum has been noted. Patients are not infrequently sent in with this diagnosis, but the vomiting quickly subsides with rest and appropriate treatment. A true toxic chorea appears to be very rare also, and it would seem that rheumatic chorea, which is not unknown in a severe and even fatal form among young, non-pregnant women, is apt to be mistaken for this condition.

Toxæmia in all its forms may be interpreted as embracing the bulk of obstetrical disasters (including abortions and accidental hæmorrhage), and indeed it is now hardly possible to see the wood for the trees. If toxæmia is a deficiency disease, what is the deficient element ? Is the deficiency in the food, or does the pregnant woman lose the power to assimilate some essential ingredient ? What other factor or factors determine the multifarious forms that toxæmia may take ? Why is the toxic element so much more lethal in some cases than in others ? Why, for example, does a post-mortem examination show profound damage to the liver and (to a lesser degree) to the kidneys, when the clinical symptoms have been almost nil ?

Until we know the answers to these questions we can hardly hope to move much further in the prevention of toxæmia. The L.C.C. clinics take the blood-pressures and test the urine regularly, weekly in the last month. We have not, however, been able to undertake routine weighing to estimate water retention. It would have to be done with such frequency and accuracy, if it is to improve on our present safe-guards, that the task is too formidable. As for diet—one would suggest that pending further research, dogmatism on detail is to be avoided. Even in six years we have seen many fads come and go, and it is difficult to relate the instance of any form of toxæmia to variations in diet. The importance of relating advice to the exigencies of a working woman's life has also been borne in on us.

We find that the medical officers attach increasing importance to early in-patient treatment at the first onset of suspicious symptoms, e.g. appearance of albumin or rise of blood-pressure, or œdema or headache. The majority of cases clear with this measure alone. There is much evidence from the study of these cases that failure to respond quickly to treatment is, in the later months of pregnancy, a very grave danger signal however slight the symptoms may appear.

A quarter of the eclamptic patients had a trace of albumin on discharge and were, of course, watched in post-natal clinics. It is noteworthy, however, that no woman who died of eclampsia had had a previous attack, and so far as the records show this is true of all the deaths from toxæmia. This tends to show that eclampsia in the first pregnancy is not of very grave omen for future pregnancies.

Hæmorrhage (Table IX).—Death from any sort of hæmorrhage in modern times has the prima-facie appearance of an avoidable accident. Hence the cases in this group call for careful scrutiny.

(*a*) *Accidental hæmorrhage :* The fact that 30·4% of our cases had albuminuria shows that the prevention of this complication is intimately bound up with that of toxæmia. It is noteworthy that in six years no woman who has attended our ante-natal clinics has died from accidental hæmorrhage. In the past three years the five who died were all emergency cases and all admitted moribund. Their histories shared the common feature of unnecessary delay in obtaining suitable treatment. Our ante-natal clinic patients wasted no time, but summoned the ambulance and put themselves into hospital as they had been enjoined to do if they felt ill.

TABLE IX.—HÆMORRHAGES. 1934-36.

Total Confinements 46,293.

Accidental Hæmorrhage.

Year	Cases	Maternal deaths	Infants' deaths: Still	Infants' deaths: Within ten days	Albuminuria
1934	86	1	37	5	33
1935	135	2 (1)*	52	21	30
1936	153	2 (3)*	67	16	51
	374	5(4)*	156	42	114
		Rates 1·3%	41·7%	11%	30·4%

* Died from other causes.

Placenta Prævia.

Year	Cases	Maternal deaths	Infants' deaths: Still	Infants' deaths: In ten days
1934	98	3	51	8
1935	129	4	53	14
1936	148	3	57	16
	375	10*	161	38
		Rates 2·6%	43%	10%

* Including 3 deaths from sepsis.

Post-partum Hæmorrhage.

1934	...	No record	
1935	...	123 cases	... 4* deaths
1936	...	181 cases	... 5 deaths (4 other deaths from unrelated causes)
		304 cases	... 9* (4) deaths
Rates	...	0·9% incidence 3% case mortality	

* 2 delivered outside hospital and admitted moribund with placenta undelivered.

(*b*) *Placenta prævia :* In a series of 375 cases we lost seven patients directly from hæmorrhage and three from sepsis, owing to attempts at emergency treatment in the home. Only one of the women who died had attended our clinic. Two of the women had an extremely sudden and violent bleeding with no warning ; in two obvious danger signals were disregarded by the medical attendant ; in one there was a dangerous complication (transverse presentation and impacted shoulder) ; and one patient refused to co-operate.

(*c*) *Post-partum hæmorrhage* has in the past two years been recorded in nearly 1% of deliveries and has been responsible for nine deaths (four other patients who had hæmorrhage died from wholly unrelated causes).

Two women were delivered outside and admitted moribund with the placenta in situ. Two had severe heart lesions and adherent placenta. One had primary anæmia and adherent placenta. One had uterine inertia, which ended in a forceps delivery. One had albuminuria and toxæmia. One had marked primary anæmia, with pink bone-marrow. One only was a normal woman with a normal confinement.

It will be noted that five out of nine women who died had an adherent, or more strictly, a retained placenta. The importance of this condition is further emphasized when one turns to the deaths from obstetrical shock (Table X). Out of 12 deaths attributable to this cause in ante-natal clinic patients, nine were associated with retained placenta. These cases are often difficult to classify as it is impossible to say how much the loss of blood has contributed to the fatal result.

In only one death out of the whole 80,000 cases was the placenta pathologically adherent (placenta accreta).

Certain conclusions may be drawn from these two groups of what may justly be considered to be preventable deaths in a wide sense.

(1) The importance of the management of the third stage. This is a very old story, but it is doubtful if it is always fully appreciated by pupil midwives and students. There is no point, one finds, on which specialist opinion differs more than in the treat-

ment of the retained placenta. How long should one wait before intervention? Is bleeding (possibly concealed bleeding), or shock from manual removal the greater risk? In our experience, all theories and all methods have their failures.

(2) The grave effects of even slight blood loss in an exhausted, nervous, anæmic, or undernourished woman is not always appreciated by the attendants. The best opinion has for long urged blood transfusion when in doubt—some authorities say if the pulse rises over 100. This useful measure can, however, be overdone, and is not devoid of risk—we have had one death this year from hæmorrhagic nephritis following a transfusion.

(3) The necessity for prophylactic blood grouping of patients likely to have complicated labour. This we have found most valuable. It has been suggested that all pregnant women should be grouped at the ante-natal clinics, but I doubt if the trouble and expense are justifiable.

(4) The importance of *unceasing* vigilance in labour-room routine for emergencies. The equipment for grouping and for transfusion should be *always* at hand, and not only got ready when trouble is expected. All staff, whether day or night, permanent or locum, junior or senior, should know exactly what is expected of them in an emergency.

(5) In the opinion of some of our staff, the use of chloroform for *full* anæsthesia in labour, as for forceps, versions, &c., is to be deprecated as likely to produce free hæmorrhage.

It is very gratifying, in view of the early records, that to date in 1937, i.e. in our last 16,000 cases, we have had no death from post-partum hæmorrhage.

TABLE X.—OBSTETRICAL SHOCK.

Years 1931-36 Total deaths, 26			Confinements 79,254
Ante-natal care in L.C.C. Clinics—12 deaths.			
Principal cause		No.	Complications
Adherent placenta			
Removed by hand introduced	5		1 Anæmia and p.p.h. 1 Pyelitis 1 Primary anæmia
Credé's method	2		1 P.O.P. and forceps 2 Primary inertia and forceps 1 Normal labour
Retained, not delivered	2		1 Marked primary anæmia 1 Acute pyelitis and forceps
		9	
Acute pyelitis, normal labour		1	
Failed forceps craniotomy		2	
		12	
Ante-natal care, other or nil—14 deaths.			
Failed forceps (before admission)		10	1 Flat pelvis 2 Large child 1 Elderly and obese mother 3 P.O.P. 3 Nil abnormal
Abnormal presentations		3	Hand, elbow, face, 1 each
Adherent placenta		1	Severe toxæmia, medical induction at 38th week
		14	

Accidents of childbirth (Table X).—(*a*) *Obstetrical shock:* These deaths fall definitely into two distinct groups, those occurring among women who have attended ante-natal clinics, and the emergencies who have had little or no ante-natal care. The first

group of cases are almost always associated with retention of the placenta, and have already been discussed. As far as the "emergencies" are concerned, one has to record a sad series of thirteen neglected or mismanaged cases. The basic trouble is usually a persistent occipito-posterior presentation or "uterine inertia", but in the final result the woman is sent in to hospital with (for example) the cervix torn off; the child's body wrenched off at the neck, the head being in situ; or the perineum torn into the rectum, while the os is still undilated, &c. These cases, together with four at least of those admitted with ruptured uterus, would give an unduly pessimistic view of modern domiciliary obstetrics if one did not remember that the series extends over six years and that London has nearly 4,000,000 inhabitants, and had in the relevant period some 350,000 births.

(*b*) *Rupture of uterus:* This series calls for special comment, as no accident of childbirth is more regrettable.

Table XI (*a*) and (*b*).—It will be noted that three of the ante-natal clinic patients who ruptured showed no adequate cause at the post-mortem examination. One of these women had had a medical induction by a routine method, including quinine and pituitrin; the two others, however, had no apparent reason at all. One of the emergency patients presented a similar remarkable condition. The remaining six emergencies were obstructed labours in mothers aged 40 or over.

TABLE XI (*a*).—RUPTURE OF UTERUS, 1931-36.

1.—*Ante-natal Care at L.C.C. Clinics—7 Deaths.*

Age	Parity	Complications
24	1	Operation for twisted ovarian cyst one year previously. Post-mortem showed old hæmatoma in broad ligament had ruptured into lower uterine segment. Death from sepsis.
34	8	Rupture of old Cæsarean scar—second operation.
38	1	Forceps delivery. Died septic peritonitis. At post-mortem found that small sharp bony tumour attached to 4th sacral vertebra had torn uterus.
36	4	Spontaneous rupture before admission shortly after onset of labour. Delivered herself, collapsed and died forty minutes later. No ascertainable cause for rupture.
40	7	No disproportion. Uterine inertia. Ruptured twenty-one hours after labour began before os fully dilated. Hysterectomy death from hæmorrhage.
39	11	Breech turned in ante-natal clinic two days before onset of labour. Uterine inertia. Adherent placenta.
43	13	Normal pregnancy and previous labours. Sudden pain after 8½ hours in labour followed by collapse. Hysterectomy and death from shock.

TABLE XI (*b*).—RUPTURE OF UTERUS, 1931-36.

2.—*Ante-natal Care other or nil—7 Deaths.*

Age	Parity	Complications
33	2	P.O.P. presentation, failed forceps outside hospital. Craniotomy in hospital and hysterectomy.
41	3	Acute hydramnios—twins—adherent placenta.
41	3	Sudden pain during labour, day before admission, admitted moribund, ? cause.
43	4	Neglected transverse presentation—fall downstairs at onset of labour.
41	5	Severe A.P.H. (marginal placenta) Version done in hospital.
45	14	Albuminuria, disproportion from large child—uterine inertia.
45	15	Placenta prævia and obstruction from hydrocephalic head.

Pulmonary embolus.—This group is much smaller than in most analyses of maternal deaths, as all deaths from emboli following uterine sepsis are allocated to the latter cause. In all cases but three the diagnosis was confirmed by post-mortem, and in those three it was considered very doubtful by the consultants who reviewed the notes. One of these deaths is referred to under spinal anæsthesia (*vide infra*).

Anæsthetics (Table XII).—The most interesting item under this heading is the mortality from spinal anæsthesia during Cæsarean section. One other death, differently

certified under the direction of a coroner's jury, was almost certainly due to this cause. In all cases the anæsthetic was given by an experienced medical officer. We have no record of the number of Cæsarean operations in which this form of anæsthesia was used, but in a series of 781 cases no other form of anæsthesia caused death.

The fatalities from chloroform and ether mixture took the form of acute pulmonary œdema supervening very suddenly some hours after a short anæsthesia in previously healthy women. One of these deaths was not recognized at the time as associated with anæsthesia.

TABLE XII.—DEATHS FROM ANÆSTHESIA, 1931-36.

Total Deliveries 79,254.

Year	Spinal anæsthesia	Chloroform	Ether	C. and E. mixture	Ether and Ethyl chloride	Indications
1931	—	2	—	2	—	1 Forceps for contracted pelvis 2 Failed forceps and shock 1 Placenta prævia; severe hæmorrhage
1932	—	—	—	(1)*	—	1 Post-maturity. Inertia, forceps, acute pulmonary œdema
1933	1 (1)*	1	—	—	—	1 Forceps: contraction, P. O. P. presentation 1 Cæsarean: contraction (stovaine) 1 Cæsarean: contraction (stovaine)
1934	1	—	—	—	—	1 Cæsarean: contraction, percaine gas and oxygen
1935	1	—	—	—	—	1 Cæsarean: contraction (stovaine, gas and oxygen)
1936	—	—	1	1	1	1 Forceps for delayed labour (rigid parts) 1 Forceps for P.O.P. presentation 1 Manual removal adherent placenta
1931-36	3 (1)*	3	1	3 (1)*	1	11 (2)*

* Probably due to anæsthetic.

The most gratifying feature is the absence of fatal, or indeed any detrimental, results reported from the cases of intermittent anæsthesia given in maternity units in the last five years. The Council has accepted the view that mitigation of unnecessary pain should be regarded as an integral part of obstetrics as it is of surgery or dentistry. After experimenting with the appointment of six specialist resident anæsthetists, powers were given to the maternity sisters and other trained midwives for the administration of chloroform in capsules and by means of the Christie Brown and Young Simpson apparatus. Latterly the Minnitt's apparatus for gas and air has proved invaluable. It is regrettable that the very effective instrument for the use of undiluted gas, designed by Professor Chassar Moir, is not yet permissible for midwives under the C.M.B. rules.

Cæsarean sections (Tables XIII (*a*) and (*b*)).—The mortality rate of a series drawn from 22 different units is necessarily higher than the rates reported by individual obstetricians or even by individual hospitals. No operation is more dramatically life-saving and few are more easily misused, as the experience of the United States shows. Technically it may be one of the easiest operations in obstetrics, but none requires greater skill and judgment to be *consistently* successful. Our improved figures probably show a greater readiness to appreciate the need for expert consultation on each case. The danger of rushing into excessive operative interference for alleged disproportion discovered at ante-natal clinics is thoroughly appreciated at our units.

The series of 87 Cæsareans for placenta prævia with two deaths (the last 57 operations having no death) may be noted.

TABLE XIII (*a*).—CÆSAREAN SECTIONS, 1931-36.

Indications and Death-rates.

Indication	1931 Cases	1931 Deaths	1932 Cases	1932 Deaths	1933 Cases	1933 Deaths	1934 Cases	1934 Deaths	1935 Cases	1935 Deaths	1936 Cases	1936 Deaths	Totals Cases	Totals Deaths
Contracted pelvis and disproportion	82	3	77	1	90	2	84	4	63	2	76	0	472	12
Obstruction from other causes ...	8	1	7	2	5	1	5	2	4	0	5	0	34	6
Extended breech	0	0	0	0	0	0	1	0	6	0	5	0	12	0
Placenta prævia ...	11	0	9	1	10	1	13	0	13	0	31	0	87	2
Concealed A.P.H.	4	0	2	2	4	1	2	0	2	1	3	0	17	4
Eclampsia ...	1	0	2	1	5	1	3	0	0	0	0	0	11	2
Other forms of toxæmia	0	0	3	1	4	2	6	3	4	2	5	0	22	8
Heart disease ...	5	0	7	1	8	1	19	1	16	2	16	2	71	7
Miscellaneous* ...	9	0	10	1	10	2	3	0	12	1	11	0	55	4
Totals ...	120	4	117	10	136	11	136	10	120	8	152	2	781	45
Percentage of total confinements ...	1·19		1·04		1·17		1·04		0·78		0·85		0·98	
Case mortality rate:														
Mother	3·3		8·5		8·6		7·3		6·6		1·3		5·7	
Infant (up to ten days)	10·0		17·1		8·0		16·0		11·6		12·5		12·5	
Morbidity rate ...	—		—		—		15·4		5·0		10·5		—	

* Includes age of mother, phthisis, psychosis, extreme obesity, concurrent diseases.

TABLE XIII (*b*).—CÆSAREAN SECTIONS, 1931-36.

Causes of Death.

	1931	1932	1933	1934	1935	1936	Total
Total sections	120	117	136	136	120	152	781
1.—Post-operative causes:							
Sepsis	3	3	1	5	—	—	12
Post-operative shock ...	—	1	4	—	1	—	6
Pulmonary embolus ...	1	1	(1)*	—	—	—	3
Paralytic ileus	—	1	—	—	—	—	1
Anæsthetic	—	—	1	1	1	—	3
2.—Other causes:							
Eclampsia	—	1	1	—	—	—	2
Other toxæmias	—	1	—	3	3	—	7
Heart diseases	—	1	—	1	3	2	7
Other concurrent disease ...	—	1	3	—	—	—	4
Totals	4	10	11	10	8	2	45

* Probably due to anæsthetic.

Deaths from associated causes (Table XIV).—Municipal hospitals of necessity find themselves burdened with a disproportionate share of labours complicated by concurrent disease, owing to the reluctance of many voluntary hospitals to admit these patients into their wards. Heart disease in a variety of forms comes to the Council's maternity units, owing to their facilities for prolonged in-patient treatment. The part played by rheumatism in this dangerous handicap to childbearing is striking, but of a series of 307 in-patient admissions for cardiac disease (mainly valvular lesions), 33% of the 129 primipara and 49% of the 178 multipara gave a definite

history of rheumatism or chorea in childhood or adolescence. The case mortality rate for primipara is 4·7% and for multipara 9·9%.

TABLE XIV.—MATERNAL DEATHS 1931-36 (AFTER THE 28TH WEEK OF PREGNANCY).

Death Due to Associated Causes.

	1931	1932	1933	1934	1935	1936	Total
Confinements	10,038	11,239	11,681	13,066	15,291	17,936	79,254
Causes :							
Valvular heart disease ...	6	5	4	7	9	3	34
Other circulatory disease ...	3	4	1	0	2	1	11
Acute pneumonia (including influenza)	10	3	11	2	4	7	37
Phthisis	4	2	5	2	4	3	20
Other pulmonary disease ...	4	6	2	3	1	0	16
Neoplasms	0	0	2	2	1	1	6
Acute inflammatory or septic conditions	1	2	1	0	1	0	5
Concurrent surgical conditions	0	0	1	2	0	0	3
Concurrent medical conditions	1	0	0	1	0	3	5
Totals ...	29	22	27	19	22	18	137

The deaths from pneumonia were mainly influenzal, uterine sepsis being in every instance excluded. It is worth noting that under the British system of computing maternal mortality an influenza epidemic may appreciably affect the maternal mortality rate.

TABLE XV.—MATERNAL DEATHS, 1931-36 (AFTER THE 28TH WEEK OF PREGNANCY).

Delivered Before Admission.

Cause	1931	1932	1933	1934	1935	1936	Total
Puerperal sepsis	18	12	13	9	5	1	58
Eclampsia	1	2	0	2	1	1	7
Other toxæmias	1	1	2	2	0	1	7
Ante-partum hæmorrhages	1	0	0	0	0	0	1
P.P.H.	1	1	1	0	0	0	3
Accidents of childbirth	0	0	1	1	0	0	2
Concurrent surgical conditions ...	—	—	1	1	—	1	3
Concurrent medical diseases ...	1	—	1	1	2	0	5
Acute prævia	4	2	0	1	0	0	7
Phthisis	0	0	0	0	1	1	2
Other pulmonary diseases	2	0	1	0	0	0	3
Puerperal insanity	0	2	1	0	3	0	6
Totals	29	20	21	17	12	5	104

Deaths of women confined before admission (Table XV).—This is a chance-selected group of no statistical value. The fall in total numbers does, however, indicate an increasing readiness to send abnormal cases into hospital earlier, which is all to the good. The drop in admissions for sepsis is due to the diversion of patients to the more suitable environment of the North Western Hospital Puerperal Sepsis Unit or the Queen Charlotte's Hospital Septic Block.

CONCLUSIONS

It is encouraging to note that although the general London rate is 15% to 20% higher than in 1936, in the first ten months of 1937 the mortality rate (excluding abortions) for the Council's hospitals has fallen by over 20%. No dramatic results can be expected, but a steady drive towards higher standards of efficiency in staffing

and accommodation, combined with that eternal vigilance which is the price of a mother's safety, should enable the municipal hospitals to take their full share in a national system of sound midwifery.

[The London County Council has no responsibility for the contents of this paper. I have, however, to thank Sir Frederick Menzies, Medical Officer of Health, and Dr. Bruce, Principal Medical Officer, for their permission to use the material, and the Medical Superintendents of the Hospitals concerned for their unfailing help and co-operation.]

Section of Dermatology

President—H. HALDIN-DAVIS, F.R.C.S.

[*November* 18, 1937]

Baron Alibert (1768-1837): His Life and Work

By J. D. ROLLESTON, M.D.

BARON ALIBERT offers an attractive study not merely to the dermatologist but also, as in my own case, to the student of medical history, as being one of the most outstanding physicians of his time.

As for many years in succession before the War I used to pay regular visits to Professor Gaucher's Clinic at the Hôpital Saint-Louis, Paris, the centre of Alibert's activity, where his memory is still evergreen, it occurred to me that a short account of his life and work might be of interest to this Section on the occasion of the centenary of his death on November 4, 1837.

Jean Louis Alibert, who occupies the same position in French medicine that Willan does among us, both being the founders of modern dermatology in their respective countries, was born on May 26, 1768, at Villefranche de Rouergue in the Aveyron Department of France—the son of a magistrate. Like Trousseau, his successor in the chair of therapeutics in the Paris faculty of medicine, he first intended to be a teacher of literature, but on the dispersal of the religious college at which he was a pupil at the time of the French Revolution, he changed his plans and took up medicine, his principal teachers being Pinel and Bichat, and his fellow-students Dupuytren and Bretonneau among others. He qualified in 1799 with a thesis on the treatment of pernicious fevers, which went through several editions, the fifth appearing in 1820. His rise in the profession was remarkably rapid, as two years after qualification he was appointed assistant physician to the Hôpital Saint-Louis and full physician the following year. This hospital, which Alibert succeeded in making one of the most celebrated dermatological centres in the world, had hitherto merely served for the treatment of "ulcers", a comprehensive term which included such heterogeneous conditions as eczema, scabies, lupus, ringworm, and syphilitic eruptions, so that it formed in Alibert's words "the sewer of all the countries in the world".

In 1806 appeared the first part of his great work on diseases of the skin under the title of "Description des maladies de la peau observées à l'Hôpital Saint-Louis et Exposition des meilleures méthodes suivies pour leur traitement". The work, of which the final part was published in 1814, was illustrated with 53 coloured plates

and was dedicated to Alexander I, the Emperor of Russia. A second edition of this magnificent monograph which cost Alibert 100,000 francs was published in 1825 and was succeeded by a smaller and much less expensive work entitled " Précis théorique et pratique sur les maladies de la peau " in two volumes in 1810–18, the " Monographie des Dermatoses " in 1832 in two volumes, and the " Clinique de l'Hôpital Saint-Louis " in 1833.

In addition to his works on diseases of the skin Alibert deserves recognition, as Molinéry has shown, for his pioneer work on hydrology. In his " Précis historique sur les eaux minérales les plus usitées en médecine " (1826) he mentions all the medical inspectors, chemists, pharmacists, and naturalists who have written on spas, and gives an account of the watering places not only in France but in all parts of the world, as well as the benefits derived by the patients at Saint-Louis from the use of mineral waters. He was also the author of " Nouveaux Eléments de Thérapeutique ", of which the first edition appeared in 1804 and the fifth in 1826, and of " Nosologie Naturelle " in 1817.

Besides these principal works Alibert made numerous contributions to periodical literature not only on dermatological subjects, but also on therapeutics, biography, and *belles lettres*. His " Physiologie des Passions " first published in 1825, of which a fourth and posthumous edition appeared in 1861, was translated into Spanish and German. This work won him the Montyon prize of 4,000 francs, which with characteristic generosity he gave to an old and impoverished writer.

In 1821 he was appointed professor of botany, but owing to the suppression of the medical faculty in 1822 he never actually occupied this chair. The following year, however, the faculty was reorganized, and a new chair of Therapeutics and Materia Medica was founded, of which he was the first occupant.

Alibert was the recipient of many other honours both at home and abroad. He was physician to Louis XVIII and Charles X, who created him a baron, member of the Académie de Médecine, president of the Société d' Émulation, Officer of the Legion of Honour, and member of the Academies of Vienna, Madrid, Turin, and Saint Petersburg and of the societies of physical sciences of Göttingen and Jena.

In marked contrast with his pupil and subsequent opponent, the somewhat puritanical Biett, Alibert was fond of the so-called good things of this life, and his dinner parties, which were attended by a somewhat mixed society, were as celebrated as Sir Henry Thompson's " octaves ".

His death, which was due to hæmatemesis caused by cancer of the stomach, took place on November 4, 1837, at the age of 69. He left a fortune of 700,000 francs and was succeeded at Saint-Louis by P. L. A. Cazenave, the author of " Leçons sur les maladies de la peau professées à l'école de médecine de Paris ".

The high esteem in which Alibert was held is shown by the obituary notices which appeared not only in France (Reveillé-Parise) but also in this country. The eminent rank which he held in contemporary society as well as an intimate picture of the man, is illustrated by the following extract which appeared in the *Gentleman's Magazine* of February 1838 where I first found the notice of his death while searching for material for the section in *Nature* entitled " Science news a century ago " : " During the period of five succeeding reigns this celebrated physician has been the confidential physician and friend of the court of Paris, and in him France has lost another of her savants. Though on the verge of seventy, he until shortly enjoyed all the haleness and spirits of a young man. In appearance he had none of the care-worn pallid physiognomy which generally distinguishes medical men and particularly those of France, but was considerably *embonpoint*, ruddy and merry in countenance as he was in conversation. In short he was one of those few with whom we sometimes meet, who seem to have the power of casting a halo of cheerfulness around them ; and this will be remembered with a pleasing regret by the numerous friends and admirers he has left behind him. His class, as a lecturer, was always full, and though often long, his

subjects from apt illustration and happy manner of delivery, were never tiresome ". The *London Medical and Surgical Journal* of November 28, 1837, p. 180, also paid him the following tribute : " We are grieved to inform our readers that Baron Alibert, the distinguished and venerable author of the splendid works on the Diseases of the Skin and on the Physiology of the Passions has paid the debt of Nature during the past week. He was for many years the most distinguished writer on cutaneous diseases in France, though inferior to our Willan and Bateman ; his work on endermoid diseases is a record of the most careful observation. He did as much, if not more, for the elucidation of diseases of the skin, than any one of his contemporaries, either national or foreign ; but he has been far excelled by MM. Biett and Rayer, whose opinions are more accordant with modern science."

In the United States, where dermatologists seem to take more interest in the history of their speciality than in this country, interesting articles on Alibert in recent years have been published by Montgomery and Beeson besides the reference made by Dr. Pusey to him in his " History of Dermatology."

In France many leading dermatologists such as Cazenave, Hardy, Thibierge, and Gaucher have paid tribute to his memory, and a richly documented Paris thesis on him by Alfaric was published in 1917. By far the most important work on Alibert, however, is the fascinating biography by Dr. Louis Brodier, physician and curator of the museum at Saint-Louis and President of the Société Francaise d'histoire de la Médecine, who has very kindly given me a copy of his work, and allowed me to reproduce one of the illustrations (fig. 1).

FIG. 1.

[*By kind permission of Dr. L. Brodier.*]

The name of Alibert is always associated with the "tree of dermatoses", a classification in which he sought to do for skin diseases what Linné and de Jussieu had done for plants. This tree, the idea of which had been suggested to him by Torti's scheme for classification of fevers, was simply a form of classification in which the trunk represented the skin, the branches the nosological families, the twigs the genera, and the leaves the varieties. The first six of the twelve families of skin diseases were arranged from below upwards on the left side and the last six from above downwards on the right (fig. 2).

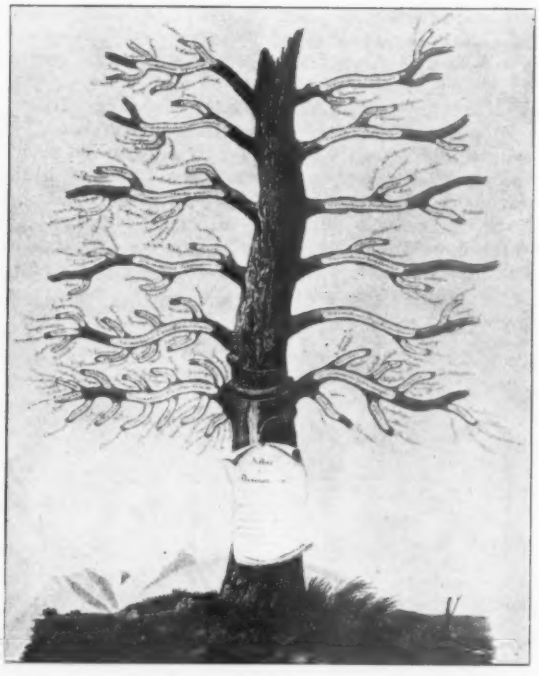

FIG. 2.
From "Monographie des Dermatoses" (Alibert) Paris, 1832.

It must be confessed that this celebrated tree did not add to Alibert's glory, but rather tended to cover him with ridicule not only from irreverent medical students, but also from dermatologists such as Cazenave and Schedel, Gilbert, Devergie, Besnier and Doyon (Brodier). The severest criticism, however, of the classification is that made by Bateman, who in the preface to his "Synopsis" speaks of it "as a splendid and pompous performance altogether destitute of method, except in the distinctions of the species under each genus". "M. Alibert", he declared, "with loud pretensions to superior skill, and much vaunting of the services which he has rendered this depart-

ment of medicine, has in fact contributed nothing to the elucidation of the obscurity in which it is veiled." Gaucher, however, while admitting that the idea of comparing a classification to a tree was not a very happy one, declared that the classification represented a great progress in dermatology, being really the first draft of a scientific and methodical study of the skin. Subsequently Alibert introduced another classification which Cazenave regarded as much inferior to the first, and to Alibert's intense chagrin a modification of Willan's classification by his former pupil Biett found more favour with the profession.

To what then does Alibert owe his high rank in the history of French medicine generally and of dermatology in particular? In the first place following the example of Desault, who founded the first clinic for surgery and that of Corvisart, who did the same for medicine, at the Hôtel-Dieu and Hôpital de la Charité respectively, Alibert established the first independent clinic of dermatology at the Hôpital Saint-Louis, where his lectures in front of the Pavillon Gabrielle were delivered during the spring and summer months in the open air like those of the ancient Greek philosophers (Alfaric). Brodier describes him as a born teacher, characterized by lucidity, method and brilliance, eager to disseminate his ideas, and benevolent to his young students. His lectures were enlivened by brilliant metaphors, quotations from the classics, and practical jokes. A prostitute with a syphilitic eruption was exhibited as "a young priestess of Venus wounded by a perfidious arrow of Cupid", and a boy with ulcerative lupus as "the victim of the bite of a devouring wolf". On one occasion, to illustrate the excessive character of the desquamation in pemphigus foliaceus, he produced a box full of scales which he showered over those next to him to the delight of those beyond his reach.

Secondly, as Brodier has pointed out, Alibert was not entirely absorbed by the study of the skin lesions in his patients, but was penetrated by the importance of internal causes in dermatology, realizing that most cutaneous affections were merely determinations to the skin of organic or humoral changes. Like Sir Erasmus Wilson[1] in this country, he held that to become a good specialist one must first learn the whole of medicine.

Thirdly, he described several new diseases, viz. mycosis fungoides, keloid, Aleppo boil, tinea amiantacea, pityriasis rubra, seborrhœa and scleroderma (Brodier). Moreover, as Sternberg has shown, he was one of the first to describe a case of acromegaly under the term of *géant scrofuleux*. Fourthly, he introduced the terms "dermatosis", "dermatolysis", and "syphilides", which found a permanent home in scientific nomenclature. His classical learning induced him to coin many more, such as melitagra for impetigo, ophlyctide for aphthæ, onygosis for affections of the nail-bed, spiloplaxie, &c., but most of his neologisms suffered the same fate as those perpetrated by his contemporary Mason Good in this country, as I have shown elsewhere, and fortunately did not survive. Fifthly, although he is not to be compared with Trousseau, his successor in the chair of therapeutics, to whom this branch of medicine owes so much, he was by no means a therapeutic nihilist. His "Élements de Thérapeutique" had no rival for over thirty years, when it was replaced by the celebrated work of Trousseau and Pidoux in 1836, and its merits were recognized by several of his successors in the same chair, namely Landouzy (1897), Gilbert (1902), and Marfan (1910). He was also the author of a work entitled "L'art de formuler" (1818), and of a historical sketch of the mineral waters most frequently employed in medicine, which was reproduced in the fifth edition of his "Éléments de Thérapeutique".

[1] "Cutaneous medicine demands, for its thorough comprehension, all that appertains to the philosophy of General Medicine, as well as the particular knowledge which belongs to the dermal textures." "On Diseases of the Skin", 5th ed., 1863. Preface.

Sixthly, he was the first to introduce coloured illustrations into dermatological works. Seventhly and lastly, he made the Hôpital Saint-Louis the Mecca of dermatologists throughout the world.

REFERENCES

ALFARIC, A. (1916-1917), *Thèses de Paris*, No. 58.
BEESON, E. B. (1932), *Arch. Dermat. and Syph.*, **26**, 1086.
BESNIER, E. (1880), *Ann de Dermat. et syph.*, n.s., **1**, 84.
BRODIER, L. (1923), J. L. Alibert, Médecin de l'Hôpital Saint-Louis.
CAZENAVE, P. L. A. (1856), "Leçons sur les maladies de la peau professées à l'école de médecine de Paris".
F. L. (1838), *Arch. gén. de Méd.*, **1**, 251.
GILBERT (1902), *Presse méd.*, **10**, 243.
GAUCHER, E. (1902), *Presse méd.*, **10**, 1095.
HARDY (1885), *Ann. de dermat. et syph.*, **6**, 629.
LANDOUZY (1927), *Presse méd.*, **5**, 805.
MARFAN, A. B. (1910), *Presse méd.*, **18**, 848.
MOLINERY, R. (1924), *Bull. Soc. franç. d'hist de la méd.*, **18**, 32.
MONTGOMERY, D W. (1929), *Arch. Dermat. and Syph.*, **20**, 506.
PARISET, E. (1837-8), *Bull. Acad. Roy. Méd.*, **2**, 164.
PUSEY, W. A. (1933), "History of Dermatology", 74.
REVEILLÉ-PARISE, J. H. (1839), *Gaz. méd. de Paris*, **7**, 193.
ROLLESTON, J. D. (1937) "The History of the Acute Exanthemata", 4.
STERNBERG, M. (1899), "Acromegaly", New Syd. Soc., 6.

Pemphigus Vegetans.—GODFREY BAMBER, M.D.

Mrs. A. W., aged 67. Four weeks ago a burning sensation began behind the right ear, and shortly afterwards small raised lumps appeared there. In a few days a similar sequence of events happened in the armpits and then in the groins.

In July 1937 the patient was severely ill with a perforated gall-bladder, which was removed.

On examination.—Raised urticarial-looking papules and plaques were present behind both ears. In the axillæ there were similar lesions and some of the plaques resembled condylomata lata. At the upper end of the inner aspect of the thighs the lesions were papules, some of which had coalesced; there were a few isolated papules on the lower abdominal wall. All the lesions were dry and there were neither signs nor history of vesicles and bullæ.

Wassermann reaction negative. White blood-cell count 8,000. (*Differential:* Polys. 68%; eosinos. 2%; large monos. 3%; lymphos. 27%.)

Histological section.—The epidermis shows a moderate acanthosis, spongiosis in places, and some migrating cells. There is a certain amount of œdema of the papillary body with an infiltration of lymphocytes, polymorphonuclear and eosinophil leucocytes, and there are also newly formed and dilated capillary vessels. The distinctive feature of the section is an intra-epidermal abscess with a great number of eosinophiles, leucocytes, and also the debris of cells.

The diagnosis suggested is pemphigus vegetans, although dermatitis herpetiformis cannot be excluded. The patient has not taken any medicine recently.

Discussion.—Dr. W. N. GOLDSMITH asked whether the question of fungous infection had been considered. He had seen cases of fungous infection causing raised, cushiony, urticaria-like lesions.[1]

Dr. GORDON said he agreed with Dr. Goldsmith, as he had seen lesions of this raised erythema multiforme type with a well-marked scaling edge from which fungus was recovered.

[1] Dr. Goldsmith has since examined the histological section and been convinced that the eruption was a variety of pemphigus vegetans.

Dr. J. T. INGRAM asked whether it was not the case that the histology of the lesion would prove whether a case was or was not pemphigus vegetans. He also suggested that this might be a toxic erythema.

Dr. I. MUENDE said he agreed with Dr. Ingram, because one of the main histological changes found in pemphigus vegetans, that of the peculiar eosinophilic degeneration of the prickle cells, was absent in this particular case.

Dr. J. E. M. WIGLEY asked whether there had been any blisters at any time.

Dr. A. M. H. GRAY said that there were true cases of pemphigus in which the vegetations started at the base of a blister. There were also cases of it in which the vegetations started on apparently healthy skin. Dr. Goldsmith had had a striking example of this latter type, in which the lesions were somewhat similar to those in this case. At the time that was shown he (the speaker) criticized the term "pemphigus" in that connexion, as he thought this name should be reserved for the former group. He thought the name "dermatitis vegetans" was preferable.

Dr. GOLDSMITH said that in his case, to which Dr. Gray referred, there had always been definite vesicles and pustules, which were sterile. In his case, too, there had been many lesions in the mouth, on the vulva, and on the fingers, and finally large plaques on the back.

Dr. BAMBER (in reply) said he had not considered the possibility that this was a fungous infection. When he first saw the patient the lesions were not epidermal. There was no change on the superficies of the skin; the lesions were urticarial and deep-seated. Apart from the illness in July, she had been in health; nothing had occurred to suggest a toxic focus, or anything to give rise to a toxic erythema. At no time had there been blisters. He understood that cases of pyodermite véjétante began, primarily, from one vesicle, caused by some external infection.

Ehlers-Danlos Syndrome.—J. E. M. WIGLEY, M.B.

This case, which I think is typical, has some unusual features.

(1) The patient's father's father, his own father, his two brothers, and one of his three sisters, were affected with what he believes to be the same condition as himself. One of his sisters, who is not affected, is married and has three children, but so far he does not know of the children being in any way abnormal.

(2) The patient shows the typical "papyraceous" atrophic scars on the forehead and on the right thigh where the skin does not lie directly over bone.

He is an apparently healthy man, aged 25. He says that all his scars have followed slight wounds. No blisters have been seen at any time. The skin round the elbows and knees is very elastic and can be drawn out to a distance of several inches; over the shoulders and chest also this over-elasticity is undoubtedly present, though much less marked. The typical broad "papyraceous atrophic" scars are present on the forehead, over the elbows, on the forearms, and the right thigh, round the knees, and on the shins. One of the knee scars is so lax as to almost form a "soft tumour" such as has been described. The metacarpophalangeal joints of both thumbs are capable of considerable over-extension, but no other joints appear to be affected.

It is of interest to note that a pyodermia affecting one shin healed in three weeks with suitable treatment.

Dr. F. PARKES WEBER said that this case confirmed the opinion that the friability of the skin and the formation of "cigarette-paper" loose scars were the most important symptoms of the Ehlers-Danlos syndrome. He supposed that scarring of the forehead would turn out to be rarer in females, as they were less exposed to bruises on the face than young males.

Telangiectasia of the Rendu-Osler Type with Camptodactylia and Muscular Atrophy in the Hands.—F. PARKES WEBER, M.D.

The patient, B. V., aged 47 years, a tram-driver, has had telangiectasia of the Rendu-Osler type for as long as he can remember, and has often had epistaxis, but he is not sure when this first occurred. The telangiectases are distributed over the face (including the ears) and the mucous membrane of the lips and nose (fig. 1). No other parts are involved excepting for ordinary De Morgan (" ruby ") spots. There is no family history of any similar condition other than that his mother, who died at about 50 years of age, had similar facial telangiectasia and suffered from epistaxis.

FIG. 1.—From a photograph taken in October 1937.

About eight years ago most of the facial telangiectases were removed by the electro-cautery, of which the scars remain ; the present ones have mostly developed since then. The epistaxis has been nearly prevented by cauterizing (with the galvano-cautery) the bleeding points in Kiesselbach's area on the nasal septum (Dr. W. Wilson), and perhaps that is the reason why the erythrocyte-count on October 26 had gone up to 5,740,000 from 4,240,000 on February 20, 1937.

The patient has camptodactylia (Landouzy's term) of both little fingers, chiefly of the proximal interphalangeal joints (figs. 2 and 3). He thinks this has nothing to do with his work as tram-driver, for he remembers having had it on the right side from the age of 14 years ; on the left side it has been present for at least some years.

FIG. 2.

FIG. 3.

He has considerable atrophy of the intrinsic muscles of the hands, which has gradually manifested itself during the last ten years, but his grasps remain fairly good, so that he can continue his work. In regard to the question of (small) 7th cervical

ribs being present to account for the atrophy of the intrinsic muscles of the hands, Dr. F. G. Wood (radiologist) reports: "The transverse processes of the 7th cervical vertebræ appear slightly larger than normal and project just beyond the transverse processes of the first dorsal vertebræ". I do not advise any operation on this account (F. P. W.).

In other respects, apart from some chronic osteo-arthritic changes in the knees and vertebral column, there is nothing abnormal (heart, lungs, abdomen, urine, nervous reflexes), and he enjoys good health. Brachial blood-pressure: 120/75 mm. Hg. Blood-serum gives negative Wassermann and Meinicke reactions. The blood-serum calcium on February 23 was rather high (112 mgm. %).

If the patient really has rudimentary 7th cervical ribs, it must be remembered that the telangiectasia is also a developmental abnormality and that the association of more than one congenital or developmental abnormalities in the same patient is by no means rare. On the other hand, the absence of pain and sensory symptoms constitutes an important, but not conclusive, point against the muscular atrophy in the hands being due to cervical ribs. On this question see especially Theodore Thompson, *Brain*, 1908, **31**, p. 295. Dr. Thompson also dealt with the developmental and hereditary nature of both rudimentary cervical ribs and atrophy of the intrinsic muscles of the hand in some cases (F.P.W. 5 Jan. 1938).

? Chronic Granuloma; ? Artefact.—CLARA M. WARREN, M.R.C.S. (for HUGH GORDON, M.C., M.R.C.P.).

The patient is a well-developed girl aged 17, employed as a clerk. She gives a history of scratching an old scar on the ankle with a knitting needle in December 1936, the ulceration appearing at the time she was under treatment for a fractured wrist in March 1937. The lesion gradually spread, although covered with occlusive bandages, and when first seen at the West London Hospital it involved the anterior surface of the ankle, and resembled a chronic granuloma. X-ray examination of the ankle-joint was negative. Microscopical examination by Dr. Waller showed denudation of squamous epithelium where there was polymorphonuclear infiltration. The main features were those of chronic inflammation of sub-epithelial tissues with fibrosis, there being no positive evidence of histological tuberculosis and no tubercle bacilli being seen. Both corneal and palatal reflexes are present. Psychological investigation revealed only that the patient is not happy at her work.

Discussion.—Dr. A. M. H. GRAY said he did not feel convinced that this was a case of artefact. He had seen a number of these cases; they had not been very fully described. He regarded this condition as chronic granuloma, due to pyococci. Chronic septic ulcers and chronic septic granulomata were not very uncommon. The proof of their nature lay in their response to treatment. When they were scraped—the sodden tissue coming easily away—and were painted with acid nitrate of mercury, the slough separated, leaving a healthy area. Some years ago he had had under his care a man who was a shunter and had knocked his elbow on a truck. A small ulcer had developed there and had gradually increased. The condition was thought to be an artefact. It was investigated from every point of view, even to the extent of searching for Leishman-Donovan bodies. Nothing positive was found and occlusive dressing failed to produce healing. After the ulcer was scraped and cauterized it healed up completely. He had seen several cases—some with frank ulcers and others with a sodden skin, which was very friable, the slightest trauma breaking it down—all of which had healed by curettage.

POSTSCRIPT.—The patient was admitted to hospital, and the lesion was scraped. The diagnosis of artefact was disproved by the subsequent course of healing (C. M. W.).

Lupus Erythematosus of the Face, with ? Lichen Planus or Lupus Erythematosus of Tongue and Buccal Mucosa.—R. D. MOYLE, M.C., M.D.

Mrs. B., aged 53, came to the West London Hospital in June 1937, skin trouble having been noticed in March. Small discoid patches of lupus erythematosus were present on the cheek, nose, and forehead. Treatment was by quinine internally and tincture of iodine applied to the margins of the lesions. Improvement took place slowly but uninterruptedly until September. On September 10 she complained of a very sore mouth. Dr. Gordon then saw her and noted "left cheek healing well, right forehead lesion improving, slight ulceration of the tongue, and white patches on mucous membranes of the cheek". The eyes were examined for retinal lesions but none was found. She has continued with the quinine and a monsol mouth-wash.

At present the tongue shows patches of leukoplakia, possibly more atrophic than is usual for lichen planus. Many of the lesions on the buccal mucosa are the white pin-head punctata of lichen planus; others, especially on the right cheek, three days ago showed superficial ulceration with a definite erythematous base and margin.

This patient presents concurrent lupus erythematosus and lichen planus lesions. Those on the cheeks, nose, and forehead are undoubtedly lupus erythematosus. Inside the mouth some lesions are typical lichen planus, but it is questionable if all are.

Discussion.—Dr. H. W. BARBER said it was usually stated in textbooks that one never saw an erosion of the surface in lichen planus of the buccal mucosa; he was sure that that was wrong. He had had several cases of undoubted lichen planus of the buccal mucosa, sometimes associated with typical cutaneous lesions, in which erosions were present.

Dr. H. SEMON said that he did not favour a double-barrelled diagnosis. He thought the diagnosis of lupus erythematosus most probable. A similar case was described and well illustrated in Zinsser's "Atlas of Diseases of the Mouth".

Maxillo-Mandibular Dermoid (or Acne Indurata).—ROBERT KLABER, M.D.

Patient a man aged 28.

Eight months ago: He first noticed a small purple nodule on the right cheek from which pus could be expressed.

Four months ago: He expressed with the pus a long coil of hair, 2 or 3 in. in length.

Two months ago: The patient was first seen, when he showed on the right cheek several small punctate scars suggesting old acne, and just below these scars two ill-defined, small, red nodules lying in the skin, each rather less than a centimetre in diameter. Their appearance, together with the presence of old acne scars, suggested the diagnosis of old acne indurata and the history of the coil of hair was ignored. He received three $\frac{1}{2}$-pastille doses of X-rays at fortnightly intervals.

Six weeks ago: The lower nodule, which was fluctuating, was punctured with the cautery.

Two weeks ago: The sinus produced by the puncture still persisted, and a long coil of hair was extracted from it.

To-day: Another coil is seen lying in the sinus. A probe may be passed up for a centimetre throughout the length of the lower nodule, but does not pass into the upper nodule.

In view of the situation of the cystic nodules on either side of the line of the embryonic maxillo-mandibular fold junctions, it seems possible that the condition might result from a dermoid cyst.

The alternative diagnosis would be ingrowing hairs entering acne indurata lesions.

Follicular Lupoid Eruption following Electrolysis.—J. T. INGRAM, M.D.

Mrs. R., aged 56, had treatment by electrolysis for superfluous hair on the face at intervals of from three to six months, over a period of about three years up to six years ago.

Twelve to fifteen months ago the present follicular, lupoid eruption of the face developed, almost confined to the muzzle area where electrolysis was performed and particularly affecting the region about and under the chin. The individual lesions have increased in size and look like typical lupoid nodules except that they are all follicular. Histological examination shows a caseating tuberculous infiltration of the usual type. The Mantoux reaction is negative in dilutions of 1 : 10,000 ; 1 : 1,000 ; and 1 : 100. Blood-count, blood-sedimentation rate, and X-ray examination of chest are normal.

A course of gold injections has been given without effect. The patient has just started general ultra-violet light therapy.

A second patient under my care, Miss B., aged 54, has an eruption exactly similar in character and distribution. She was shown at a meeting of the Section by Sir Ernest Graham-Little in October 1926.[1] The eruption has not altered since that time but the patient was not able to attend to-day. She had electrolysis fourteen years ago and the eruption appeared eighteen months later.

This patient had received some ultra-violet light treatment and treatment by freezing with carbon dioxide snow without benefit.

In March 1935 Dr. Barber showed a case under the name of rosaceous tuberculide, upon which I commented at the time.[2] His patient had had electrolysis and showed a very similar eruption to that in the present case.

Discussion.—Dr. BARBER asked whether any new lesions had developed in this case.

Dr. INGRAM (in reply) said that the patient had only been under his observation six months, and no further lesions had developed during that time. In the other case the condition had developed very little since Sir Ernest Graham-Little had shown her eleven years ago.

Dr. BARBER said he considered that the lesions were characteristic lupus nodules, in spite of the negative Mantoux reaction. Would it be advisable to destroy the lesions by diathermy ?

Dr. H. SEMON asked if the cases described had had electrolysis by the same operator.

Dr. DYSON (Manchester) suggested using tuberculin ointment 10% (i.e. the old Koch's tuberculin, 10% in vaseline).

Dr. GOLDSMITH said he questioned whether that treatment was likely to be effective, in view of the negative Mantoux reaction.

Dr. AGNES SAVILL said that she usually destroyed lupus nodules by diathermy, inserting the monopolar needle deeply and using a good strong spark. The patient felt this very little.

POSTSCRIPT.—The Mantoux reaction in the second case is positive.

N.B.—I have ascertained that both patients received electrolysis treatment from the same operator (J. T. I.).

Sclerodactylia.—HUGH GORDON, M.C., M.R.C.P.

History.—The patient, a woman aged 38, was, ten years ago, admitted to the West London Hospital on account of exophthalmic goitre and tachycardia. She had had X-ray treatment of the thyroid and had been discharged apparently cured. Four years ago she noticed coldness of the hands and face during the winter. Three years ago the fingers began to be stiff ; since that time ulcerations have appeared on the

[1] *Proceedings*, 1926, **20**, 102 (Sect. Derm. 32).

[2] *Ibid.*, 1935, **28**, 1168 (Sect. Derm., 52).

fingers and ankles. Otherwise she feels in good health and leads an apparently normal life, though somewhat crippled by the condition of her hands.

On examination.—The hands are in the inwardly bent position and are completely immobile. The skin is visibly stretched on the fingers and hands, which have the appearance of being shrunken. There is no palpable induration anywhere on the hands. There are numerous " starlike " scars on the dorsal aspects of the fingers. Abnormal pigmentation is present over the backs of the hands and wrists. There is a well-marked feeling of induration on both forearms on palpation. There is no pitting on pressure. The feeling is more of sclerodœma than actual sclerodermia, i.e. the induration feels as though it were involving the subcutaneous tissue more than the cutis. There are no signs of Raynaud's disease, nor is there any history of vasomotor symptoms. The feet are normal : a large trophic ulcer is present on the left ankle. There are no visible varicose veins. Both legs give a slight suggestion of the same induration as that on the forearms. The face has a slightly mask-like appearance. There is exophthalmos, the nose is shrunken and well-marked compensatory furrows are present on the upper lip and, slightly, on the chin. The skin of the face appears taut but there is no feeling of induration. The rest of the body is normal.

Wassermann reaction negative. Blood-count normal. Blood calcium, 8·9 mgm.%. X-ray examination : Chest normal. Hands and long bones " No bone absorption; arthritic change present ". Biopsy as yet unobtainable.

On first seeing this case four weeks ago I considered it to be a typical case of Sellei's acrosclerosis. The appearance of the face seemed to be identical with that shown in Sellei's article (*Brit. Journ. Derm. and Syph.*, **46**, 531). According to Sellei, the essential characteristics of arteriosclerosis are symmetrical and simultaneous changes in the hands, face, and feet, these changes being essentially a process of shrinkage and contraction. Vasomotor symptoms are common, so is ulceration and so are the star-like scars on the hands, which do not occur in sclerodermia. The phalanges become sharpened and ulcerated and the bones of the fingers dry up. These bone changes are pathognomonic for acrosclerosis. The phalanges are frequently hard to the touch and this hardness is not due to the induration and in most cases extends only to the terminal phalanges. In this respect it differs from true sclerodactylia which has its origin in sclerodermia. In true sclerodactylia the changes spread from the arms to the back of the hands and thence to the fingers and not in the reverse direction.

After reading Sellei's article again carefully, I came to the conclusion that if Sellei's differentiation of this condition was to be accepted then this case must be classified as a sclerodactylia due to a localized sclerodermia, since in this instance the process began as a sclerodermatous condition of the forearms and then spread forward to the fingers.

In addition there are no bone changes nor is there any rise in blood-calcium. In every other respect, however, the condition conforms exactly to the description of acrosclerosis. Possibly the two conditions—acrosclerosis and sclerodactylia—are not so sharply differentiated as Sellei thought them to be.

Discussion.—Dr. BARBER said that a point of interest was that the thyroid condition had been treated with X-rays. He believed this to be a characteristic case of sclerodactylia, and he wondered whether there was a connexion with the thyroid disease.

Dr. F. PARKES WEBER said he regarded this as a typical case of what he would prefer to call the sclerodactylia type of sclerodermia. The symptoms seemed to coincide with those of published cases, and with those which had been shown from time to time at meetings of the Section. He did not agree with the attempt which had been made to make a separate group of acrosclerosis.

? Parapsoriasis: Case for Diagnosis.—HUGH GORDON, M.C., M.R.C.P.

History.—The patient, a healthy man aged 30, was first seen in April 1937, having what appeared to be a fairly extensive pityriasis rosea with large elements; the lesions were markedly pigmented. Slight pruritus was present. There was no history of any drug having been taken.

Ultra-violet light was given and this increased the general pigmentation of the body but appeared to cause the scaly lesions to disappear gradually. The eruption, however, was still present in July, three months later. A holiday sun-bathing cleared the skin completely on the sun-exposed areas, though lesions are still present on the bathing-trunk region. Since the patient's return fresh lesions have been occurring over the whole body.

On examination.—There is general pigmentation, more to the waist than on the bathing-trunk area. In the axillary region there are fawn-coloured plaques with a little scaling. On the bathing-trunk area some of the original circular scaling lesions are still present. On looking at them closely it can be seen that they consist of little shiny-topped confluent papules with an adherent scale. On the trunk are many pigmented stains which mark the site of similar lesions. By reflected light a general reticulated lichenoid appearance can be seen over most of the trunk. The mucous membranes are clear.

I have called the condition parapsoriasis because I am unable to offer any better diagnosis. I am, however, grateful to Dr. Goldsmith for reminding me of a condition described by Gougerot as "papillomatose confluente et réticulée". So far as my memory serves, Gougerot's description fits this particular case fairly adequately.

Discussion.—Dr. BARBER said he thought that this patient had had an eruption which might be termed pityriasis lichenoides acuta.

Dr. INGRAM said he would have thought that the pigmentation was against the diagnosis pityriasis lichenoides acuta. He regarded the case as one of pityriasiform lichen planus.

Dr. A. M. H. GRAY agreed with Dr. Ingram; the eruption was of the type which Dr. Whitfield had called the erythematous type of lichen planus.

Dr. W. DYSON also thought that the condition was lichen planus.

Dr. BARBER did not think the lesions on the arm could be called lichen planus.

Dr. W. N. GOLDSMITH agreed that the eruption was suggestive of lichen planus, but it bore a close resemblance to pictures of Gougerot and Carteaud's papillomatose confluente et réticulée.[1] The histology should be a great help, because in papillomatosis there was no infiltration in the corium, and practically no acanthosis. It was almost entirely a hyperkeratosis.

Dr. I. MUENDE said that the "Papillomatose papuleuse confluente et réticulée" described by Gougerot, was essentially a papillomatosis and its main histological characteristics were acanthosis with some hyperkeratosis. In the "Nouvelle Pratique Dermatologique" its description followed on that of acanthosis nigricans which it resembled in some degree.

A case shown at the last meeting as ? mycosis fungoides had been considered by members to be one of widespread acanthosis nigricans, but was, in his (Dr. Muende's) opinion, probably a case of Gougerot's disease.

POSTSCRIPT.—A subsequent biopsy rules out the diagnosis of lichen planus and suggests parapsoriasis.—[H. G.]

[1] *Arch. f. Derm. u. Syph.*, 1932, **165**, 232.

Xeroderma Pigmentosum.—A. M. H. GRAY, C.B.E., M.D.

A. J., a male aged 18, has suffered from this condition since childhood. I have been unable to interview his parents and he is not very intelligent—consequently the history is meagre. He remembers that the skin of his face and limbs has been freckled and has had warty nodules on it since he was 7 years of age, and that at this age a nodule appeared on the left eyelid and fell off. About a year ago another swelling began on the same eyelid and grew to the present size. The patient lives in the depth of the country and has worked on a farm in Wales: apparently he has not sought advice for the condition until quite recently. The parents are not blood-relations and he has no brothers or sisters. So far as he knows, no other member of his family is similarly affected.

Xeroderma pigmentosum.

I am showing the case on account of the extensive epitheliomatous changes which have taken place in the lesions on the face. The eruption otherwise shows the ordinary characters of this rare disease. The skin, from the middle of the arms to the tips of the fingers, and from the middle of the thighs to the middle of the legs, is studded with small brown pigment spots, and a great many warty keratoses are present. The skin of the face and neck shows the same picture, but in addition there is a fungating tumour, the size of a plum, completely occluding the left eye, and a

large number (some twenty or so) of other epitheliomatous growths of varying type are scattered over the forehead, cheeks, and chin. There is also a warty growth in the concha of each ear. Some of the growths have the clinical characters of rodent ulcers, with a raised, smooth, pearly border ; others are fungating growths of varying size, mostly covered with a blood-stained crust, while two show ulcers with sharply-cut margins, without any swelling or obvious infiltration of the margins. The cornea of the right eye is opaque.

It is proposed to remove the greater part of the mass over the left eye by diathermy and to treat the growths by radium.

Discussion.—Dr. F. PARKES WEBER asked whether there was any proof that shielding from the sun saved these patients from the lesions of the disease. Radcliffe Crocker had pointed out (in his textbook) that in true xeroderma pigmentosa the disturbance was not entirely limited to the areas of the body which were exposed to sunlight.

Dr. W. DYSON said that many years ago he had been taught that in cases of this kind when the patients were protected from bright sunlight, the condition became quiescent and ceased to progress, but they did not become well. He learned also, that when epitheliomata had once formed they had to be dealt with. He did not know whether this teaching still prevailed.

Section of Therapeutics and Pharmacology

President—J. W. TREVAN, M.B.

[*December* 14, 1937]

The Introduction of New Remedies into Clinical Practice

PRESIDENT'S ADDRESS

By J. W. TREVAN, M.B.

IN some ways I suppose the layman would regard this Section as one of the two most important Sections of the Royal Society of Medicine, as it devotes itself entirely to the subject of treatment. Most of the others are concerned largely with the very difficult problems of preventive medicine, the scientific natural history of disease, or the art of diagnosis. The layman has very little conception of the immense amount of labour involved before rational treatment can begin, but sometimes I wonder whether the profession spends as much energy on the science of therapeutics as it does on the other ancillary sciences of medicine.

It has been said before that medicine itself is an art, not a science. I think perhaps it might be well to try to make clear what I mean by a "science." A science is a description of natural phenomena and their interrelations as determined either by observation, or if possible—and preferably—by experiment. Some sciences by their very nature are almost entirely observational, such as astronomy. A description of the relation of the phenomena must be in such terms, particularly where experimental observation is in question, that it conveys to the reader, solely by the statement of the observed facts, the conviction of its truth. Proof of the scientific proposition must be objective and not depend on the opinion of the observer or his undescribed previous experience, or on the reputation of the observer himself. It is, of course, a fact, that like all other activities of the human mind, such an abstract ideal is not always attained. Some degree of prejudgment by the reader still affects the opinion which he forms of a scientific paper. If the President of the Royal Society describes a startling new discovery it is more likely to be accepted by the scientific world than if it is described merely by the President of the Section of Therapeutics of the Royal

Society of Medicine, but the aim of all scientific workers is the production of purely objective reasons for a belief in certain interrelations between natural phenomena.

It is hardly necessary to say that if a patient comes to one of us with a lump on the back of his neck, a purely objective description of the phenomena is not in the least what he wants from us. What the patient wants is the application of all the knowledge and experience of the physician to the relief of his condition. He would probably be better pleased if the lump could be charmed away by an incantation than if it were cured by some procedure based on proper scientific evidence, but the application of scientific evidence to the treatment of the lump is not science, any more than driving a locomotive is science. There is a science of diagnosis, of pathology, of therapeutics, but the actual treatment of an individual is not a science. That does not mean that a physician should not be a scientific worker, even in his daily task, nor does it mean he will not be a better physician if he is a scientist too.

This Section is composed of people who believe that the treatment of patients would advance more rapidly and more certainly if the procedures used in treatment were subjected to the most rigid and exhaustive examination and control. It is a regrettable fact that the science of therapeutics is still in its infancy. No great generalizations such as the atomic theory, or the structure of the benzene ring, or the theory of evolution, have as yet appeared in pharmacology. A large number of remedies which cannot be spared from the Pharmacopœia have been introduced on purely empirical grounds; and it cannot be finally predicted from their structure and action on animals that the latest products of modern scientific chemistry are worthy of final admission to the physician's bag until direct trial is made on man. There is still an empirical element in the adoption of new remedies, but there is empiricism *and* empiricism. All sciences pass through an empiric stage, which differs from pure empiricism in that the observations and experiments are tabulated and controlled, and allowed to speak for themselves.

Primitive man seems to have taken by mouth—and would probably have given himself by hypodermic injection, had he had a syringe—every product of Nature which was soluble or readily reduced to a powder. This habit led to the discovery of cinchona, digitalis, ergot, belladonna, opium, ephedra, and many others. That is a good bag for pure empiricism. But in all ages there have been individuals who have in some sense been scientists, in that they have been less impressed than their fellows by the weight of tradition and authority, and have allowed the facts of their observations to speak for themselves. The alchemists gave us antimony as a by-product of their mystic search. Fowler's analysis of an ordinary quack remedy of the eighteenth century started arsenic on its brilliant career, but what may be called the really scientific era did not begin until the end of the eighteenth century.

The first step was to start the removal from the Pharmacopœia of the drugs which owed their position to superstition of various kinds. That process was effectively begun by William Heberden; it is not yet complete. The next step began with the attack of the chemist on the problem of isolating pure active principles from the various plants in use.

Quinine, for example, was discovered in 1792, and for some years the resources of the developing science of chemistry were applied to the isolation of active principles from these vegetable drugs in common use. The earliest systematic pharmacological examinations of alkaloids were carried out by Magendie about 1821. One curious fact comes out in the examination of all the work on alkaloids, namely, that in no

case I know of has a useful alkaloid been extracted from a plant for which some preparation has not previously been used therapeutically.

This stage in the application of scientific methods to medicinal agents might be called the purely analytical stage. It resulted in the production of many active principles, some of which were in a form more convenient to administer and more constant in composition, such as morphine. Others, such as cocaine and atropine, found uses not contemplated in the original prescription of the drugs.

The hunt is not yet finished, although the number of new useful alkaloids obtained grows less and less every year ; ephedrine and ergometrine are examples of the latest of this group.

In the forties and fifties, ether and chloroform were introduced on a basis of experiment on man. It was 1862 before chloral was introduced into medicine, and not until we reached the eighties that the modern spate of new synthetic organic preparations began to flow.

More modern developments in therapeutics fall into three groups : the first, those arising from the working-out of the facts of immunity to bacterial products ; the second, the development of hormone and vitamin physiology ; and the third, which in some cases overlaps the second, the production by organic chemists of synthetic remedies of all kinds, some on the basis of modifications of normal constituents of the body and some entirely new products which have certain desirable actions in disease.

The first group—antitoxins, antisera, and vaccines—has given us some valuable remedies. Its contribution to therapeutics has been less dramatic than had been hoped. The introduction of these substances into therapeutics has been the result of much careful and accurate scientific work in the laboratory, but too often the scientific excellence of this preliminary work has not been maintained in the final steps of clinical application.

The evidence, for example, for the usefulness of Type I pneumococcus antiserum in pneumonia, produced by Bullowa and Cecil in America, is better evidence than the experiments in the laboratory which led to the discovery of this serum. These workers, by the use of proper untreated controls, have settled for all time that there is a high probability that serum produced by the injection of pneumococci into horses will save some cases of pneumonia from death. I do not mean to say that anti-pneumococcal serum is more useful in pneumonia than, for instance, antidiphtheritic serum is in diphtheria—its effect is in fact disappointingly small—but that some patients may be saved by it can be regarded on the work of these observers as an established scientific fact.

It is especially illuminating that the discovery of the exotoxin of the *Streptococcus hæmolyticus* was delayed for many years because of the insensitivity of laboratory animals to this toxin ; it was only when man was used as the experimental animal that the production of an antiserum followed. The efficacy of antiserum in scarlet fever and the efficacy of the immunization of man with the toxin has been demonstrated with a reasonable degree of scientific probability. Rabbits can be saved from the acute death which follows the administration of a virulent culture by the use of the antitoxic serum, so that a trial in septicæmic conditions seemed justified, but for some years there was a division of opinion as to whether this serum was of any value in streptococcal septicæmias as distinct from scarlet fever. A control series of cases has now been published by Colebrook, who goes so far as to say that antitoxic serum is harmful in septicæmia. Such controlled experiments on man are extremely difficult to obtain—and the more difficult, the more potent the new remedy. A few dramatic recoveries after the administration of a new remedy is apt to raise in the

mind of the physician a feeling that he is failing in his moral duty to his patients if he does not treat every case with it. I would, however, press for the adoption of rigid controls at all times. It is most urgent that we should be able definitely to say a remedy is effectual before adopting it permanently. A few apparently favourable cases may only be a statistical accident, and it is not fair to impose useless remedies on an indefinite succession of patients. I think the physician has a duty to the community at large in the treatment of the individual, and accurate knowledge of the worth of a remedy can only be finally obtained by subordinating some individual patients for the time to the general interest of sick people as a whole. I would point out too, from the point of view of duty to the patient he is treating at the moment, that he is not certain that the administration of any new product will be harmless to that patient ; if he is prepared to take the risk of administering a new product to a series of patients, he should be prepared to take the risk of withholding that remedy from some patients until there is same degree of probability, greater than about ten to one, that the material is active. A pure statistician would be horrified at taking any action on a probability of ten to one, and if the evidence available is only that of one series of experiments which is not backed up by laboratory or clinical evidence of a different kind, this degree of significance is inadequate.

Unfortunately this branch of therapeutics, which began so well, has given birth to a large number of products for which the scientific laboratory evidence is dependent solely on analogy and not on direct experiment, and the clinical evidence on impressions produced in the minds of susceptible physicians by entirely uncontrolled experiments. Vaccination against colds is perhaps the most dreadful example of the misapplication of scientific observations in this field, and various products of dried, ground, frozen, or hydrolysed bacteria are still offered with all the advertiser's power of panegyric, and all his glib falsification of the results of evidence obtained for quite different products taken from quite different bacteria.

We will now look for a moment at the second group, that of the hormones and vitamins. Adrenalin is apparently well established in the therapeutic armamentarium. Curiously enough its place in therapeutics is distinct from that of all the other hormones except posterior pituitary ; it is used for local actions in concentrations which it never reaches in the body, and might quite well have been introduced into therapeutics as the result of the labours of synthetic chemists, even if it had not been discovered to be a constituent of the adrenal medulla. The active substance of posterior pituitary is also in the same position ; there is not much evidence that the posterior pituitary secretion of a normal body has any physiological function in connexion with the uterus, although it is possible that Krogh's theory of its toxic action on the capillaries is a true one.

The place of thyroid is completely established ; I think no scientific worker could quarrel with the experiments most of you have probably carried out on your own patients with myxœdema, and no one would quarrel with the view that dry thyroid does what is said of it in the textbooks of medicine. This is an example of a drug for which the provision of objective and scientifically acceptable evidence is comparatively easy, for since myxœdema is not a fatal or rapidly progressing disease, the patient can be made to serve as his own control by noting the effects of discontinuing treatment.

The introduction of insulin is almost a perfect example of the way in which a new remedy should be brought into use. The original idea that the use of fœtal pancreas would prevent the destruction of the insulin in the course of preparation was worked out by Banting, on animals ; biochemists were called in to investigate the problem of removing trypsin from the extracts of normal pancreas. The product was tested on rabbits and diabetic dogs, under the control still of the original discoverer, and the

early clinical results were obtained in close collaboration with the physiologist. Material was not set free for issue as a commercial product until the most stringent proof of its clinical value was obtained. Here again it was perhaps easier than in some cases to obtain adequate clinical evidence because of the relatively chronic and constant course of the disease for which it is used.

It is perhaps too early to assess the clinical value of the sex hormones and of preparations of anterior pituitary, but the claims of the vendors of these considerably antedated any reasonable evidence of their usefulness. The vitamins have their special uses well established for A (nightblindness), B (beri-beri and pellagra), C (scurvy), and D (rickets). Vitamin A is also recommended for protection against infections such as colds, on the basis of experiments on rats grossly deficient in Vitamin A, in which the infective condition is quite different in character. Ignoring the *non sequitur* in the evidence, is anyone in my audience sure that a sound collection of results can be produced to support this view? Vitamin B is now recommended for constipation. Here some animal evidence can be advanced for its use, but is there anywhere an account of the comparison of a series of cases taking excess of Vitamin B with an exactly similar group on an ordinary representative diet?

The last group of drugs are those produced synthetically. Any attempt to deal in a detailed fashion with the group is impossible. The happy hunting ground of synthetic chemists for years was the barbiturate acid derivative. With monotonous regularity a new barbiturate was periodically announced, which was always more easily tolerated than any before, so that either veronal was an exceedingly deadly weapon or the more modern variations are quite non-toxic—if we believe the advertisements. Of this group few have had any sufficient evidence, either laboratory or clinical, to justify their general distribution in preference to older remedies. Vaso-constrictor drugs have also proved tractable to molecular modifications; I suppose the number recommended is at least equal to the number of large "fine-chemical" manufacturing firms in existence. Yet all was not waste in the work on either of these two groups, for out of one came the short-acting anæsthetics and out of the other benzedrine, both with unlooked-for properties. Chemotherapy is now one of the chief growing-points of therapeutics, and with the attack on bacterial diseases by chemical means well under way, medical men may look forward to a considerably larger daily postal budget.

Alongside the real advances brought about by all these various activities there is another and more reprehensible one. Of old, doctors were recommended to use remedies because the gods willed or the planets directed. To-day such practices have been given up as superstitions, but like the demoniac in the parable, the therapeutic house, cleaned and garnished, is in danger of being occupied by seven worse devils. Every day our post-bags are deluged with blurbs of preparations in which the ancient superstitions are replaced by pseudo-scientific jargon. Statements are made with bland assurance which are demonstrably untrue.

Mixed up with such stuff are reasoned and not unscientific recommendations of new and old drugs of proved value, with all graduations between the two extremes. But the rubbish outweighs the good, and it seems that although we are in sight of the purgation of the Pharmacopœia from the remnants of the first dark ages of therapeutics, a new dark age is setting in, and the shelves of our pharmacies are filling up with preparations whose claims, though veiled in scientific terms, are based as much on superstition as those of mithridatum itself. And of all superstitions the pseudo-scientific superstition is the blackest.

These stupidities have often been pointed out by others—but who is to blame for them? The amount of money spent on them must be enormous. The money is

spent by business concerns which must make a profit or succumb. They do not want to throw money away on advertising, so presumably it pays to write advertisements in the terms of which I have complained. I hate to draw the obvious conclusion that the medical profession gets the advertising it deserves. Like all polite people I "except present company". All of you, I expect, will agree with some of my criticism of advertisements. But the existence of these advertisements must mean that there is a response by some part of the medical profession. May I produce another piece of evidence to support this view? I took one number of a leading English medical journal and tried to classify the advertisements of remedies appearing therein. There were forty-three such advertisements. Judging by the most lenient standards, I found only twenty-seven for which it might be claimed that they were based on some foundation of laboratory and/or clinical fact. Thirteen were untrue, misleading, or simply silly. Three I could not classify because they appeared under proprietary names and gave no sort of idea of the composition of the material. That, of course, is based on my personal judgment, but I tried to be as lenient as possible.

I did a control experiment by taking the *Journal of the American Medical Association* and repeating the process. I found only thirteen advertisements of medicinal agents, of which I should have rejected only one on the criteria used for the English journal. I suppose that the welter of cult medicine in America has made the medical profession examine its beliefs with more care than we have used. I commend the process to your attention; I would ask you to scan the advertisement pages of any English medical journal and ask yourself what is the justification for the use of each preparation. I think that for most of my audience the results would indicate a proportion of unjustifiable remedies not greatly different from that which I have given. Whether, if all your results were put together, the drugs rejected by all of you would be as great in number as I have indicated is another question, but I think some of them would certainly not meet with approval from any medical man present. The state of the advertising literature in this country therefore suggests to me that the medical profession is not sufficiently critical of the claims made for a new preparation. The useless preparations, it may be argued, do no harm, and in any case the physician has to treat his patient—he has to practise his art. In the practice of an art of any kind traditional procedures and procedures based on vague personal beliefs are always in use, but the constant endeavour of all modern arts and crafts is to substitute an accurate scientific control for tradition and vague opinion. It is, I suppose, inevitable at the present stage of therapeutics that many things should be done to patients for which strict scientific justification cannot be produced, but I would ask that it should be done with open eyes, and that the medical man should be quite clear in his own mind when he is acting on established fact and when he is *faute de mieux* using some scientifically unjustifiable method. I think some of the confusion arises from the neglect of pharmacology, or, if you like the words better, the science of therapeutics. Ever since the separation of pharmacology from physiology, about in the sixties of the last century, and until recently, the main task of the pharmacologist has been to pour cold water on the claims made for most of the remedial agents. Such a form of activity tends to result in the unpopularity of its author, and I think the present status of pharmacology in this country is the reflection of this unpopularity. Whatever the cause, it seems to me that the provision in this country of scientific work on the actions of drugs ought to be greatly increased. In too many centres of medical education the space devoted to pharmacology and the quality of the equipment are grossly inadequate for the carrying out of much more than the exiguous demands of the present teaching courses.

May I express my regret that in the London School of Hygiene and Tropical Medicine and the British Post-Graduate School such a department has as yet not been considered necessary. I would put it with all deference that in post-graduate education particularly, a department in which it was a chief concern of the teacher to provide a critical estimate of the many new drugs which are appearing would be of great value. The department of the science of therapeutics should be the pampered darling of any medical school. As much money should be spent on it and on the provision of its apparatus as on the dissecting-room, and as much time should be devoted to it as is now devoted to anatomy. I can hear some of my audience calling on heaven to help the unfortunate student, but I think there are still things that might be left out of the curriculum. Do I hear another remark to the effect that the whole clinical side of the hospital is a therapeutic laboratory? That is true only in a limited degree. The proper object of the hospital ward is the practice of the art of medicine; the science of therapeutics must always take a subsidiary place. Not only so, but the introduction of new remedies involves a vast amount of work of a preliminary kind which can only be carried out in the laboratory, and the introduction of the student to scientific methods of thinking is better separated at first, as everyone will agree, from the confusion introduced by the practice of an art. If this increased attention to pharmacology could be given, I believe we might see a more critical spirit grow up in the profession as regards the introduction of new remedies. My impression is that the subject is better dealt with in America than in this country, and the steady flow of new and brilliant discoveries from across the Atlantic is perhaps evidence in favour of this view. I believe the matter is really urgent. There is no doubt in my mind that we are at the beginning of a new era in therapeutics, when the number of useful tools will be multiplied greatly. Unless some academic institutions outside the urgencies of competitive commercialism are established on a larger scale than at present, treatment is likely to be swamped under a mass of good, bad, and indifferent material provided by the manufacturers and accepted uncritically by the profession, and the second dark age of therapeutics may be worse than the first. The near future will see the establishment of the scheme of therapeutic research under the ægis of the Government and that scheme is most welcome, but it will not provide the second requisite, the forming of a proper therapeutic outlook in the minds of the budding practitioner. I hope I am not being too critical of the work of the physician; the difficulties surrounding his task are immense, and no one has a higher admiration for the devotion and skill with which he carries it out than I have, but I think he must devolve some of his labour on a pharmacological colleague, who should be treated not as a necessary evil to be accommodated upstairs somewhere, but as a colleague who is one of the most essential links in the education of the student in the science of therapeutics.

To turn to the manufacturer. In what I am going to say about him I would like to make it perfectly clear that I am expressing only my private and personal view as a citizen of a democratic country. A large number of the remedies introduced in past years, either in the shape of improvements on treatments discovered in academic laboratories, or entirely new products, have been the result of prolonged and very costly investigation in the private laboratories of the firms themselves; the cost of such researches has to be met by the sale of the products made by the firm; it is indeed to be doubted whether money could have been found for the production of the many valuable new remedies except by manufacturing firms. The difficulties of the economic question are great, and I would ask manufacturers to inquire whether they have not been sometimes more eager to realize a cash return than to be certain that the drugs they produce really do what is claimed for them. They may reply that that is not strictly their function. If they are challenged about any particular drug

they can nearly always produce a letter or a short article, the essence of which is generally " I have used this preparation in an inadequate number of cases without any control and most of the patients got better ". If the doctor wants the material to treat his patients with, who are the manufacturers to say he should not have it ? I find it extremely difficult to counter this argument, but I think that even if we grant that to provide, for the use of some practitioners, material which the majority consider useless, is a perfectly worthy method of making money, it is not right to advance claims in advertising literature which cannot be strictly supported by good evidence. There is, in fact, an improvement of recent years in the advertising literature of the more important firms, but for some there is a long way to go yet ; it is to be remembered that a large part of the education of the medical profession in the use of new drugs, in fact the major part, is carried out through the medium of advertising literature or the visits of commercial travellers. I suggest that manufacturers should try to make their literature suitable for such a high mission.

Another source of confusion and error is the devotion of manufacturers to brand names ; it is inevitable that in the present state of the nomenclature of organic compounds some trivial names should be invented for new synthetic products. One cannot expect practitioners to talk about para-aminobenzenesulphonamide, but this product, besides the now almost universally accepted term " sulphanilamide ", appears under a host of different trade names, some of which are misleading, and when used in the medical literature leave one uncertain as to what particular chemical compound is the subject of the report ; dealing, as I do daily, with this subject, I myself find it extremely difficult to remember which is which. This problem could be partially solved by the establishment of some semi-official body which would assign trivial names to a new preparation, but it will not be entirely solved until the manufacturers agree to give up the use of registered names entirely. There has been some movement in this country towards the establishment of a Committee that would assist the practitioner to recognize, amongst all the things that are offered to him, those which have a sound basis of evidence. The list of New and Non-Official Remedies of the American Medical Association is, I think, performing a very useful function, in spite of some matters of terminology that might perhaps have been dealt with differently. Before a drug is admitted to that list the manufacturer has to submit evidence on which claims made for it are based and, what is most important, agree to the publication of any report on it, whether favourable or unfavourable. Whether the law of libel in this country would permit the publication of some of the caustic comments which are made in the *Journal of the American Medical Association* may be open to doubt, but perhaps unfavourable reports could be suppressed in this country in the English fashion. When the practitioner has been educated up to give preference to drugs on such a list, some of the things I have been complaining about should disappear.

One other reprehensible practice which must be mentioned is the use of obscure, often slightly inaccurate, chemical names in the descriptive literature for some preparation, to conceal the fact that it is only some well-known drug masquerading as a new product. Amidopyrin is one of the drugs which is fairly frequently subjected to the process, on which comment is superfluous.

One of the evils of competition is the multiplication of the production of and research on new remedies by competing manufacturers. It is an evil which cannot be entirely avoided where production is in the hands of private enterprise, and it has some compensations. The stimulus of competition does increase the speed with which new remedies are made available for general use. The disorganization and readjustment necessary in a drug-producing organization which is brought about by

the process of substitution of one remedy for another would, in some cases, if the production of drugs was in the hands of one organization, inhibit the desire of the producer to make available a new remedy; but I fear under present conditions the stimulus of competition often results in the profession being assailed with more new remedies than can be properly tested. No firm can keep entirely out of this race for priority; if it acts on the basis of not supplying material until proper clinical trials have been carried out, it is likely to have great difficulty in catching up with the competitor who is less scrupulous, and it will find itself labelled as unprogressive and old-fashioned. Not only so, but I understand that it is characteristic of purchasers of remedies, that if they are attracted by some new product they are apt to transfer their custom in other staple products to the firm that has provided the new one.

I have mentioned the barbiturates as a group in which this competition has been pronounced; the sulphanilamide group is another in which a similar situation will arise—if, indeed, it has not already arisen. It is possible to produce drugs of the sulphone or sulphonamide group showing activity equal to or better than that of sulphanilamide, at a rate far greater than they can possibly be tested on man. Mr. Gray and Dr. Smith of the Wellcome Foundation have synthesized some fifty-five compounds, at least half of which have an activity greater than, or not greatly inferior to, that of sulphanilamide as judged by experiments on infected animals. We know over one hundred and forty—and I expect the number is much greater—of which the proportion of active substances is about the same. There are indications that the inhibition of streptococcal septicæmia in mice is not an entirely accurate guide to the relative activity of the drugs of this group in man. The final assessment of the therapeutical value of this group can therefore only be carried out on man. The task is an enormous one and is not rendered easier by the feeling of large numbers of practitioners that sulphanilamide, or one of the derivatives of it on the market, is an entirely adequate drug. If we look closely at what has happened it will be seen that there is a large element of empiricism in the introduction of sulphanilamide itself; it was placed on the market long before any adequate clinical trials were reported, on the basis of its resemblance in the laboratory to red prontosil. It almost seems as if, for this particular group, attempts to produce a new and better preparation than sulphanilamide would be better suspended for a time, whilst the pharmacologists get down to the task of discovering how it works. If they succeed, the hunt for a new remedy on the basis of that knowledge could be reopened; but this will be a task of which the duration cannot be foretold.

No discussion of this kind would be complete without a reference to the Therapeutic Trials Committee. It is doing extremely valuable work, and it is to be hoped that its activities will be extended, and that manufacturers will make increasing use of its services. Can we hope for a time when no new remedy will be introduced until it has been passed by the Therapeutic Trials Committee? Perhaps this is an impossibility, but it would certainly do away with many of the abuses and illogicalities of which I have complained.

To sum up: I feel we are at the beginning of a new age in the production of remedies for the treatment of disease; that the present training of medical men in therapeutics is inadequate to give them that judgment which is necessary to enable them to sort out the good from the bad in the flood of preparations presented to them; that the establishment of more centres of research is necessary, in which new remedies can be assessed independently of the work done in commercial laboratories; that the standards of advertising literature are too low, and that some censorship should be established by the profession itself; and finally, that the manufacturers themselves

might consider the possibility of submitting all important new remedies to the Therapeutic Trials Committee.

In conclusion I would like to say that I know I am talking with the outlook of a laboratory worker. You would perhaps be justified in saying that it is easy for such a one to criticize his clinical colleagues—I am well aware of that. I am not sure that my choice of career was not largely determined by the fact that I found clinical medicine much too difficult, but I do believe that what I have said does represent not unfairly what must rapidly become an intolerable position, unless something is done about it.

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Section of Urology

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Vesical Exclusion

PRESIDENT'S ADDRESS

By HENRY WADE, C.M.G., F.R.C.S.

ABSTRACT.—In the operation of vesical exclusion the urine stream is deviated from the urinary bladder into the colon, thereby forming a cloaca, or on to the surface of the skin, where a fistula discharging urine is created.

The operation is indicated in all cases of complete or partial vesical exstrophy. It is successfully employed in treating severe cases of vesico-vaginal fistula, whether the result of obstetric injury or the delayed action of radium.

In carcinoma of the urinary bladder, whether primary or secondary, it is practised, frequently preliminary to the operation of total cystectomy.

In cases of persistent vesical systole and in intractable cystitis, it has also been occasionally done.

The immediate operative mortality following transplantation of the ureters into the pelvic colon is largely dependent on the condition for which the operation is performed. In cases of malignant disease it is high: whereas in conditions that are non-malignant it is a relatively safe procedure.

The establishment of a cloaca, particularly in the female, of itself produces no appreciable disability. If the operation has been performed for a congenital or an acquired deformity, and this has been skilfully and successfully carried out and the patient has become stabilized, the expectancy of life should not be appreciably diminished.

The case of a patient, upon whom the operation had been performed twenty-nine years previously, is reviewed and particulars of others in which it was performed fourteen years ago, or later, are referred to.

In the pre-operative preparation, in addition to the usual thorough clinical investigation, an examination by excretion urography is indicated, especially to determine the possible presence of a third ureter or a single functioning kidney. At this period it is also important, particularly in cases of obstetric injury, to be sure that the rectal sphincter is fully competent and that no hæmorrhoids are present.

The operative technique was carried out under twilight sleep and spinal anæsthesia. The vital importance of careful post-operative treatment is emphasized. By the immediate post-operative administration of sodium sulphate, by intravenous injection and attention to other details, bilateral ureteral transplantation carried out in one stage could be safely embarked upon without the fear of anuria developing.

A detailed record of 60 cases, in which the operation of vesical exclusion has been carried out by the author is given.

RÉSUMÉ.—Dans l'exclusion opératoire de la vessie, l'urine est conduite dans le colon, avec formation d'une cloaque, ou à la surface, où elle s'échappe par une fistule urinaire.

L'opération est indiquée dans tous les cas d'extrophie totale ou partielle de la vessie. On l'emploie avec succès dans les cas graves de fistule vésico-vaginale, qu'elle soit le résultat d'un traumatisme obstétrical ou d'un effet tardif d'un traitement au radium.

Elle s'emploie dans le traitement des cancers primitifs ou secondaires de la vessie, souvent comme préliminaire à la cystectomie totale.

Elle a aussi été employée de temps en temps dans les cystites obstinées et dans la systole vésicale persistante.

La mortalité immédiate suivant la transplantation des uretères dans le colon pelvien dépend en grande partie de l'affection pour laquelle l'opération est employée, étant élevée dans les cas de tumeur maligne et relativement basse dans les cas bénins.

La formation d'une cloaque, surtout chez la femme, ne cause pas d'inconvénient appréciable. Si l'opération est habilement et soigneusement exécutée dans un cas de malformation congénitale ou acquise, et si le malade s'est habitué à son nouvel état, sa vie moyenne n'est pas appréciablement raccourcie.

L'auteur rapporte un cas opéré il y a 29 ans, et fait allusion à d'autres cas opérés il y a 14 ans ou moins.

Une pyélographie excrétoire est indiquée avant l'opération en plus de l'examen clinique complet habituel, surtout pour exclure la possibilité de la présence d'un troisième uretère ou d'un seul rein fonctionnant. Il est aussi important, surtout dans les cas de traumatisme obstétrical, de s'assurer en même temps que le sphincter rectal fonctionne bien, et qu'il n'y aie pas d'hémorroïdes.

L'opération se fait sous le sommeil crépusculaire associé à l'anesthésie spinale. L'auteur appuie sur la grande importance du traitement post-opératoire. Si le danger d'une anurie est évité par l'administration iptravéneuse de sulphate de soude immédiatement après l'opération et par l'attention à quelques autres détails, la transplantation des deux uretères en un temps pourra être entreprise avec sureté.

L'auteur rapporte en détail 60 cas personnels d'exclusion opératoire de la vessie.

ZUSAMMENFASSUNG.—Bei der operativen Blasenausschaltung wird der Harn von der Harnblase unter Bildung einer Kloake in das Kolon oder zur Hautoberfläche geleitet, wo er sich durch eine Fistel entleert.

Die Operation ist in allen Fällen von totaler oder partieller Blasenexstrophie indiziert; ferner wird sie mit Erfolg in der Behandlung schwerer Fälle von Blasen-Scheiden-Fistel angewandt, gleichgültig ob sie durch Geburtstrauma oder als Spätwirkung einer Radiumtherapie aufgetreten ist.

Sowohl bei primärem als auch bei sekundärem Blasenkarzinom wird diese Operation vorgenommen u.zw. häufig als Vorläufer einer totalen Cystektomie.

Gelegentlich wurde sie auch in Fällen von hartnäckiger Blasensystole oder schwer behandelbarer Cystitis vorgenommen.

Die unmittelbare Sterblichkeit durch die operative Verpflanzung der Harnleiter in den Beckenteil des Kolons ist weitgehend von dem zugrundeliegenden Zustand abhängig, wegen dessen die Operation vorgenommen wird. In Fällen von bösartigen Tumoren ist sie gross während in nicht bösartigen Fällen die Operation ein verhältnissmässig gefahrloser Eingriff ist.

Die Schaffung einer Kloake an sich verursacht besonders bei der Frau keine besonderen Beschwerden. Wenn die Operation wegen einer angeborenen oder erworbenen Deformität vorgenommen und geschickt und erfolgreich ausgeführt wurde und der Patient sich an die neuen Verhältnisse gewöhnt hat sollte die Lebensdauer nicht merkbar beeinflusst werden.

Der Fall eines Patienten, bei dem die Operation vor 29 Jahren vorgenommen wurde, wird geschildert und Einzelheiten anderer Fälle, die vor 14 Jahren und später operiert worden waren, werden besprochen.

Bei der Vorbereitung zur Operation ist abgesehen von der üblichen gründlichen klinischen Untersuchung eine Untersuchung mittels Ausscheidungspyelographie indiziert, besonders auch um das eventuelle Vorhandensein eines dritten Harnleiters oder einer einzigen funktionierenden Niere festzustellen. In diesem Stadium ist es ferner besonders in Fällen von Geburtstrauma wichtig sicher zu sein, dass der Mastdarmschliessmuskel voll funktionsfähig ist und dass keine Haemorrhoiden vorhanden sind.

Die Operation wird unter Dämmerschlaf und Lumbalanaesthesie ausgeführt. Grösster Nachdruck wird auf sorgfältige Nachbehandlung gelegt. Die unmittelbar nach der Operation vorzunehmende intravenöse Anwendung von Natriumsulfat und die Beachtung anderer Einzelheiten ermöglicht es die doppelseitige Ureterenverpflanzung in einzeitiger Operation ohne Risiko und insbesondere ohne Gefahr der Anurie vorzunehmen.

Verf. gibt einen ausführlichen Bericht über 60 eigene Fälle von Blasenausschaltung.

INDICATIONS

EVERY now and then a case is met with in which the urinary bladder has ceased to do its duty and will no longer hold water. A number of causes may produce this sad state of affairs.

Congenital malformations.—(1) Complete vesical exstrophy: An error in development during intra-uterine life may result in the child being born with a strawberry-like swelling on its lower belly wall, and when this swelling is examined it is found to be the posterior wall of the bladder bulging forwards unsupported, the anterior wall of the bladder being absent, as is also the anterior abdominal wall in this region. Water weeps in a constant steady stream from the under-surface of this swelling and when it is tilted up by the finger the two ureteral orifices are seen jutting forth urine. The bladder here fails to function, as there is no bladder cavity.

(2) Subsymphyseal vesical exstrophy: Another less obvious error in development is that in which the anterior wall of the bladder and the anterior abdominal wall are

formed naturally, but the bladder neck is wanting in front, the condition being known as subsymphyseal vesical exstrophy, or epispadias in the female.

Instead of being obvious at birth, the possessor of this deformity may grow up to adolescence without the true nature of her disability being recognized. As an infant and young girl, the patient is considered as suffering from lack of control of micturition from a nervous or similar cause.

The explanation of this oversight is due to the fact that Nature has here formed a urinary bladder which is a saucer capable of holding some water when the patient is in the recumbent posture (fig. 1), but which spills its contents when she assumes the erect posture. Thus she may reach the age of 17 or 18 years before it is recognized.

FIG. 1.—To illustrate the "saucer bladder" in a case of subsymphyseal vesical exstrophy in a young woman. Excretion urography photograph at thirty minutes; patient recumbent. J. D., aged 17.

When she is then examined, as she lies in the dorsal position with the thighs together, at first nothing abnormal is noticed except that the lower margin of the mons veneris is notched. When the thighs are separated the nature of the deformity is apparent. The notch previously seen is observed to deepen into the cleft which splits the clitoris and passes down to the neck of the bladder, the anterior wall of the urethra being absent, as is also the vesical neck in front, so that the examining finger passes readily through a wide patulous orifice into the bladder cavity. The vesical neck in front and the anterior wall of the urethra may alone be absent in the simplest variety of this deformity, as illustrated in figs. 2 and 3.

In the majority of these cases an X-ray examination shows that the symphysis pubis has failed to unite.

Obstetric injury.—Vesico-vaginal fistula: Sometimes during parturition the urinary bladder is so severely damaged that a large opening into the vagina results; a vesico-vaginal fistula is formed. Fortunately the great majority of these cases can

be repaired by plastic operation. Sometimes this treatment fails and a large fistula remains through which every drop of urine escapes to foul the vulva and excoriate the thighs of the unfortunate patient.

In still another variety of vesico-vaginal fistula the vesical sphincter may also be damaged so that even a successful attempt to close by plastic operation the fistula fails to cure the patient as incontinence from another cause still remains.

Vesical carcinoma.—In the light of our present knowledge we have to acknowledge that there are still cases of primary carcinoma of the urinary bladder, the only cure for which is by removing the entire organ, doing the operation of total cystectomy, and

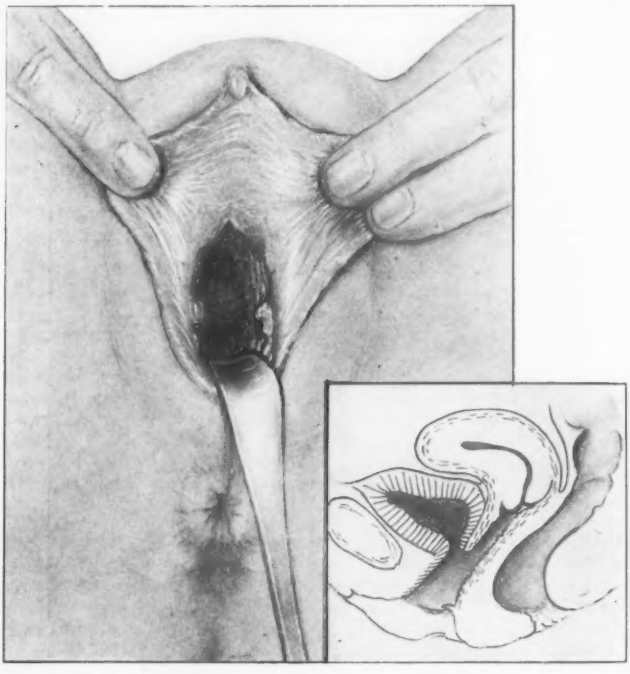

FIG. 2. FIG. 3

FIG. 2.—To illustrate the malformed patulous bladder neck in a case of subsymphyseal vesical exstrophy in a young woman. The labia minora are separated and retractor inserted into the vagina, revealing a deep transverse ridge extending across the cavity; in front of it is the patulous bladder neck and behind it the vaginal cavity. J. D., aged 17.

FIG. 3.—Diagram to illustrate the anatomy in the case of subsymphyseal vesical exstrophy sketched in fig. 2. J. D., aged 17.

this of course necessitates the previous deviation of the urine stream by vesical exclusion.

Carcinoma of cervix uteri treated by radium, followed by vesico-vaginal fistula from delayed action of radium.—Carcinoma of the cervix uteri is most successfully dealt with by the application of radium. In many cases a permanent cure is effected, leaving the patient without any apparent disability. Unfortunately, this is not so in every case. In more than one I have seen this treatment followed by destruction of the bladder floor and the creation of a vesico-vaginal fistula owing to a delayed action of the radium. These cases are unsuitable for cure by a plastic operation and are best treated by vesical exclusion.

Recurrent carcinoma of cervix uteri.—The fate of the urinary bladder is also raised in carcinoma of the cervix uteri which has been overlooked or has recurred after treatment.

This disease spreads upwards behind the bladder along the cellular tissue planes of the pelvis so that it comes to surround and involve the lower ends of the ureters and subsequently the wall of the bladder. To attempt to destroy this growth by radiation would necessitate a partial destruction of the bladder floor and the production of a vesico-vaginal fistula.

If untreated, the expectancy of life in these cases is stated to be from seven to nine months, death being frequently due to anuria.

In treating them the first problem is therefore that of performing the operation of vesical exclusion by deviating the urine stream. Thereafter treatment by radiation can be actively carried out regardless of the extent to which the now functionless bladder is damaged. Or, if so desired, the growth may be excised by combined hysterectomy and cystectomy.

Tuberculous cystitis.—Persistent vesical systole : Vesical exclusion may be called for in the treatment of tuberculous disease of the urinary tract. The accepted treatment of unilateral renal tuberculosis is to remove the diseased kidney and ureter by operation. When this is done, in the majority of cases the bladder is found to be the site of tuberculous cystitis. A natural cure of this usually follows within two years after the operation of nephrectomy. When this cure is not achieved the inflamed bladder remains in a state of persistent systolic contraction, with the result that backward pressure is exercised on the solitary kidney, and hydronephrosis and hydroureter develop, with progressive impairment of renal function, culminating ultimately in uræmia and death. Having witnessed this tragedy on several occasions, I have tried to relieve the deadly backward pressure by various means—by drainage of the renal pelvis, by drainage of the ureter, and by sympathetic denervation of the lower end of the ureter. These have afforded only temporary relief, so that ultimately it was recognized that vesical exclusion was indicated and in certain of these cases the single ureter was transplanted into the pelvic colon.

Intractable cystitis.—I have carried out the operation of vesical exclusion, transplanting the ureters into the pelvic colon, in the treatment of cases of intractable cystitis—a procedure which at first sight some might consider unjustifiable. In each of the cases ureteral transplantation was only finally decided upon after the patient had received prolonged treatment by a physician widely experienced in the treatment of such cases. It was only when he also finally confessed failure that the treatment was decided on. In all these cases the patients had a normal and uneventful convalescence and are in excellent health to-day, happy, and deeply grateful for the treatment they have received.

Urethral stricture with urethral and vesical fistulæ.—In three cases classified under this category I have been driven to perform the operation of vesical exclusion, transplanting the ureters into the colon as a forlorn hope. Two were cases of fracture of the pelvis in young lads, with rupture of the urethra followed by extravasation of urine and pelvic cellulitis. After many operations and years of suffering, they were broken-down in health, with several vesical and perineal fistulæ. It seemed to me that the only hope of improving their lot was by deviation of the urine stream into the bowel.

Another case of urethral stricture had been followed by destruction of the urethra and development of numerous fistulæ with intractable cystitis above.

Spina bifida with vesical incontinence.—I have had one case of this nature. It illustrates the desperate problems that are laid before you when you are known to be interested in the subject of vesical exclusion. The case sent to me was that of a child who suffered from spina bifida and vesical incontinence, for the relief of which the ureters had been transplanted on to the abdominal wall a year and a half before. The child was leading a life of indescribable misery. The entire urinary secretion

flowed on to the abdominal wall; the infant came to me in foul-smelling rubber clothing, and when this was removed the skin beneath was seen to be the site of an encrusting urinary dermatitis—a desperate situation. The skin was improved by baths and similar treatment, but the only hope of relief appeared to be by deviating the urine stream into the pelvic colon.

Immediate Operative Mortality

The cases I have mentioned, and particularly the last group, raise the question as to the immediate operative mortality of such an operation, the disability, if any, the patient subsequently labours under, and, finally, the expectancy of life thereafter.

As regards the immediate operative mortality, I will later give an accurate statistical record of the patients I have treated. But I would here say that my personal experience is that the most important factor in this connexion is the presence or absence of malignant disease. If malignant disease is present the mortality is high, and if your experience of this operation is to be confined to such cases you are fated to have many disappointments for, undoubtedly, your greatest triumph will be in those other cases that I have mentioned. The manner in which patients in these cases behave is such as to convince me that in all cases of malignant disease a deadly secret subtle poison is present which conspires to bring about a fatal issue. It is not in the first few hours or the first few days that disaster arises. It is later, when your other cases would have been considered safely out of the wood, that the malignant case slips back and slowly sinks. And you may lose your patient possibly, even as I did in one of my cases, by what amounted to the manifestation of the instinct of death. She ceased to talk to her relatives who sat by her bedside; she ultimately refused food, and finally death supervened. At the subsequent post-mortem examination there was no demonstrable complication present. If I may use a hackneyed and much misunderstood expression, from the surgical standpoint the operation had been most successful. All that was apparent was the malignant disease in the pelvis, for which the original operation had been performed, and this has held good in a number of other cases of malignant disease that I have dealt with. A fatal issue has ultimately supervened, usually about the third week, the post-mortem appearances, from the surgical standpoint, being satisfactory.

On the other hand, where the operation is performed for any of the other non-malignant disabilities, the immediate mortality is low.

Future Disability

The disability, if any, under which these patients subsequently labour from the establishment of a cloaca, falls now to be considered. As you are aware, many animals possess this, and in the mammalian kingdom the echidna and the duck-billed platypus are so constructed. This common channel, into which the intestinal, urinary, and genital secretions are discharged, is so regulated that segmental function is established. A "urodæum" is formed where the urine is collected (fig. 4), and a proctodæum where the intestinal content is gathered. Very soon a similar state of affairs is established in your patients. In female patients it is most noticeable. They tell you that they sleep the whole night through undisturbed and void urine three or four times during the day. They will probably mention that on many occasions it is a clear urinary secretion which is passed and that a separate act of defæcation takes place where a formed motion is evacuated. To them their existence is a natural and happy one and compatible now for the first time with full social enjoyment.

In the case of male patients, as you can understand, the nature of the act of micturition is most materially altered, but otherwise the cloaca functions as already described. Most of the women who will come under your care will be in the full vigour of their sexual life, and it is important to remember that the operation of ureteral transplantation in no way stands in the way of pregnancy, and a successful confinement. I cannot quote a case in support of this statement, but in this respect our luck has been unfortunate. In one case, that of a married woman on whom the

operation of vesical exclusion by ureteral transplantation was performed, for a vesico-vaginal fistula, pregnancy subsequently occurred ; an accident unfortunately here induced abortion. Another who had successfully and uneventfully reached her fifth month had gestation terminated by her medical adviser who, remembering her terrible experience when she had had the difficult labour which led to the vesico-vaginal fistula, thought it in the interests of her health to carry out this treatment. Personally, I was keenly disappointed as I did not share his opinion on this question. Nevertheless, I look forward confidently to tangible proof of my contention at an early date.

Expectancy of Life

To some the creation of a cloaca may seem so unnatural a process as to be incompatible with a reasonably long expectancy of life. The uninformed pessimist is apt

Fig. 4.—To illustrate the "urodæum". A collection of urine in the bowel after bilateral ureteral transplantation performed nine years previously, delineated by excretion urography. J. McD., aged 26.

to bemoan the likelihood of the early development of an ascending renal infection, suppurative pyelonephritis, and death. My personal experience is to the contrary. Sufficient years have now elapsed to enable me to give it as my opinion that if bilateral ureteral transplantation has been skilfully performed for a congenital or acquired deformity and the patient, having come successfully through the operation, has become stabilized thereafter—I mean by this that a normal functioning "urodæum" has become established—the expectancy of life has become little if at all reduced and a normal, useful, and contented life has been made possible, despite the profound physiological alteration brought about by the surgical intervention. The best illustration I know of this is the following :—

Case of Mrs. Robertson

At a meeting of the American Surgical Association held in Denver, Colorado, in June 1911, Sir Harold Stiles read a paper on "Epispadias in the Female and its

Surgical Treatment, with a report of two cases ".[1] The patients were aged 3 years and 7 years respectively, and Sir Harold had operated on one in 1907 and on the other in 1908, for the congenital malformation to which we have previously referred as " subsymphyseal vesical exstrophy ", that malformation in which the neck of the bladder is deformed, the urethral channel absent, and the vesical sphincter non-functioning. In these two cases he transplanted the ureters into the pelvic colon, doing the two-stage operation with an interval of from three to six weeks between the implantation of the right and the left ureters into the pelvic colon. The method he employed consisted of introducing the divided ureter into the lumen of the colon through a small punctured opening, the ureter being held in position by a temporary fixation-stitch of catgut, after which it was buried in the outer coat of the bowel as the rubber tube is buried in the wall of the stomach in a Witzel's gastrostomy. Both cases did well, and in the concluding paragraph of his paper Sir Harold Stiles wrote :—

> " While it would be rash to assert that my two patients will remain free from any kidney infection, it is nevertheless very satisfactory to know that more than three years have elapsed without either of them showing the slightest evidence of such a complication."

It is my good fortune to be able to give you a report on one of these cases, twenty-nine years after the operation. The patient is now a married woman, aged 32, living a happy natural life in the County of Fife. A few years ago she developed acute appendicitis and was operated on for this in hospital, and those who then cared for her were not aware that she was in any way abnormal. Her health to-day is good. By blood examination the renal functional activity is found to be normal, and examination by excretion urography shows the size, situation, and contour of both kidneys to be normal (fig. 5). The renal pelves and ureters are also normal. Even if her case stood alone, it would be sufficient to provide an unanswerable argument in favour of the contention that the creation of a cloaca by the deviation of the urine stream into the lower bowel is compatible with long life, good health, and happiness. But her case does not stand alone. Many now share her good fortune.

My earliest case was twelve years ago in a young woman aged 17 who also suffered from subsymphyseal vesical exstrophy, which had been overlooked until that date. Bilateral ureteral transplantation was carried out in two stages. Her health to-day is normal. Her kidneys are undamaged, uninfected, and functioning naturally. Many other cases now provide similar testimony.

Pre-operative Preparation

If it be granted that the operation is indicated, certain points in the pre-operative preparation should be attended to. In addition to the customary thorough medical examination, the functional activity of the kidneys should be carefully determined. The collection of a sample of urine is usually difficult and a satisfactory cystoscopic examination, with ureteral catheterization, is frequently impossible. I have found that a blood examination, with an estimation of the blood urea and creatinine, has been a satisfactory means of determining the health of the kidneys.

Examination by excretion urography.—An examination by excretion urography should be made in every case. It provides another excellent test of renal function. It will also demonstrate the possible presence of the not unusual deformity of double ureter on one or both sides. It is very important to make this observation before the operation commences, as it is very easy to overlook, in the operating theatre, the presence of a third ureter, as in a case referred to me by a colleague, in which, after the apparently successful transplantation of both ureters into the colon, urine still continued to escape through the vesico-vaginal fistula. In this case a third operation was performed by myself, and revealed a second ureter on the left side which had previously not been suspected ; on the transplantation of this into the colon, no

[1] *Surg., Gyn. and Obst.*, 1911, **13**, 127.

further escape of urine through the vesico-vaginal fistula took place, and the patient was finally cured.

The excretion urography examination will also provide a guide as to the possible presence of a single functioning kidney, a congenital malformation which, I consider, occurs in one out of every hundred normal persons. The presence of this abnormality is revealed by the excretion urography examination outlining a healthy kidney and pelvis on one side and an entire absence of shadow on the other. But in this connexion a fallacious interpretation may easily be made.

The operation of ureteral transplantation, as has been mentioned, is sometimes done in cases of carcinoma of the urinary bladder. In certain of these cases the

FIG. 5.—Photograph delineating by excretion urography the kidneys, calyces, pelves and ureters fifteen minutes after the injection of uroselectan B, twenty-nine years after bilateral ureteral transplantation into colon. Mrs. R., aged 32.

growth not infrequently involves the lower end of one or other ureter and thereby produces backward pressure on the kidney above. In such cases backward pressure, moderate in amount and even of short duration, may result in a kidney appearing to be functionless on excretion urography examination, no shadow being thrown on that side, an appearance similar to that already met with in the single functioning kidney. In such a case it is only when the abdomen is opened that it is possible to determine the cause of the absence of shadow. Where this is due to backward pressure, it is usually noted that the ureter on this side is markedly dilated and the renal pelvis tensely distended. In such a case, although even a definite degree of hydronephrosis and hydro-ureter may be present and the kidney be apparently functionless, when the pressure is relieved, functional activity returns, and even a

mild degree of hydronephrosis may be recovered from after ureteral transplantation. Another point that is here brought out is that ureteral transplantation is still possible when the ureter appears to be very grossly distended, for when it is opened and the pressure within released, it is noteworthy and satisfactory to observe how its thin walls collapse to a calibre that renders transplantation not difficult. At the same time, of course, there are cases in which the excretion urography examination reveals a degree of dilatation of renal pelves and of ureters which is bilateral and so gross that ureteral transplantation into the pelvic colon is obviously contra-indicated. I would go to the length of saying, however, in the doubtful case, when the single dilated ureter is demonstrated by excretion urography, of recommending operation and, granted that when it is exposed its walls although tense are thin, I would transplant it into the colon with every confidence.

The pre-operative preparation of the bowel is naturally of very great importance and should be carried out by the nursing staff with the thoroughness customary in all cases of abdominal surgery. Personally, I have always obtained in the operating theatre an empty, quiet, normal colon, usually contracting as a spinal anæsthetic has been employed, and one to which it has never been necessary to apply a clamp for fear of contamination of the wound. Personally I would never approve of any technique wherein an attempt is made to cleanse the bowel by lotion or by gauze swabs in the operating theatre.

It is important to remember that in cases of severe vesico-vaginal fistula produced by difficult labour, there may also be damage to the rectal sphincters and a tendency to rectal incontinence. Before the operation of ureteral transplantation is undertaken in these cases, this point should be carefully looked into and if necessary corrected. Similarly hæmorrhoids, if severe, may cause irritation, and frequently after the establishment of a cloaca. These also should be treated.

Operative Technique

In the choice of operative technique a wide field exists. Personally, I have now come to adopt, with certain minor modifications, the Coffey-Mayo operation—the Coffey No. 1 technique, as it is sometimes called. It appears to me to be the best, the No. 2 and No. 3 Coffey operations being, in my opinion, unsound in principle and inferior in many ways. The fundamental essentials of such an operation—and these apply to the wide field of abdominal surgery—are briefly as follows :—

First, as regards the anæsthetic : I prefer that the patient should come to the operating theatre unconscious of the surroundings, as previous mental anxiety and strain are undoubtedly factors deleterious to a good and speedy recovery. Twilight sleep is therefore induced. At one time I used nembutal ; in my hands it proved excellent in some cases, uncertain in others. I have therefore come back to the method of scopolamine and morphine—the adult patient receiving $\frac{1}{4}$ gr. of morphine and 1/100th of scopolamine two hours before the operation, followed by $\frac{1}{6}$th morphine and 1/200th scopolamine half an hour before going to the theatre.

The anæsthetic used in the theatre must possess one essential characteristic, i.e. it must be certain to produce complete muscular relaxation so that the operative technique can be carried through, as all modern surgery should be, on a sound physiological basis. Bacteriology is of importance in the operating theatre, but should not now have the priority we used to afford it. Like the anatomical basis of operative work as carried out by the masters with whom we served our apprenticeship, it now takes a subordinate position. The physiologically minded surgeon realizes how abundant are the harmful nerve impulses that radiate from tissues torn by self-retaining retractors, the damage to organs rich in sympathetic innervation that " packing off " produces, and the torn endothelial surfaces which such treatment results in.

The spinal anæsthetic I personally use is spinocaine, preceded by an injection of ephedrine to keep up the blood-pressure. Complete anæsthesia is thus obtained

for one hour, which is more than sufficient time to carry through the operation with thoroughness and deliberation.

The question to be next decided is whether it is necessary to do the operation in two stages—first, one ureter being transplanted into the colon, and the other being similarly treated a fortnight or three weeks later. Until a few years ago I would have had no hesitation in answering that, where time permitted, the two-stage operation was always advisable. To-day my answer is different. I now recommend bilateral ureteral transplantation in all cases—a change of opinion brought about essentially by the work on anuria and its treatment by the intravenous injection of sodium sulphate, by my young colleague Ian Lawson Dick. The sequence of events that led up to our altered decision came about when we were concerned with the treatment of malignant disease of the urinary bladder. I have always felt that the cystoscopic appearances alone were not sufficient to warrant the grave operation of total cystectomy. Before so momentous a decision is reached the bladder must first be opened, and the growth seen, felt, and examined. If the decision is in favour of cystectomy, the bladder must first close naturally, the ureters then be transplanted individually and finally the operation of total cystectomy be carried out, the procedure consuming much valuable time and requiring four separate operations—a terrible ordeal for even the most robust to go through. To shorten this technique we instituted bilateral transplantation, with immediate intravenous infusion of sodium sulphate solution and normal saline. So satisfactory did we find this in promoting immediate renal secretion and preventing anuria that we have now adopted this technique as a routine procedure in all cases.

I do not propose to describe the technique of the operation in detail. There are, however, some points I would mention. I would again remind you of the great importance of delicate handling of the tissues. When the patient is fully anæsthetized by twilight sleep and spinal anæsthesia, the abdomen, being completely relaxed, is opened by a mid-line infra-umbilical incision. The operating table is then further tilted so that the small intestine falls out of the pelvis and the field of operation is freely exposed. The right ureter is first sought for, just below the iliac vessels. Often it is seen contracting beneath the pelvic peritoneum. The peritoneum over the ureter is incised and the ureter, along with the para-ureteral tissue, is isolated down to its lower end. The lower end is now ligatured and above this the ureter is divided by means of the diathermy current, the object of employing this being to seal off the para-ureteral lymphatics as these might be a potential path for the spread of infection. The ureter, having been isolated below from the floor to the pelvic brim, is now lifted into the abdomen and the divided pelvic peritoneum is sutured. I would advise that the left ureter be sought for below, not above, the pelvic colon (fig. 6). It is much easier to find it here. It is treated similarly, but after it is isolated up to the lower surface of the pelvic colon a pair of strong curved forceps is passed along beside the ureter behind the pelvic colon to the root of its mesentery where the points of the forceps are forced through the peritoneum. Down the channel thus formed another pair of forceps is passed and the end of the divided ureter is grasped and drawn up so that it now emerges through a small opening at the root of the mesentery above the pelvic colon (fig. 7). The ureters are then prepared for implantation by the insertion of a wick of catgut up the lumen, as originally suggested by Charles Mayo, and in doing this I employ the neat device of threading the end of the catgut, acting as a wick, on to the eye of a probe, and passing this probe up the lumen of the ureter, so that it unthreads itself and leaves the catgut as a wick in good position.

In choosing a site for implantation the object is ultimately to form a "urodæum," and the best situation for this is in the pelvic colon, not in the rectum. The left ureter is first implanted high up in the pelvic colon, the right lower down. When doing this, remember that in Nature the ureters not infrequently enter the cloaca with a mucous valve protecting the outlet, and that in other cases a nipple valve projects into the lumen—and make your implantation accordingly, with the ureter running

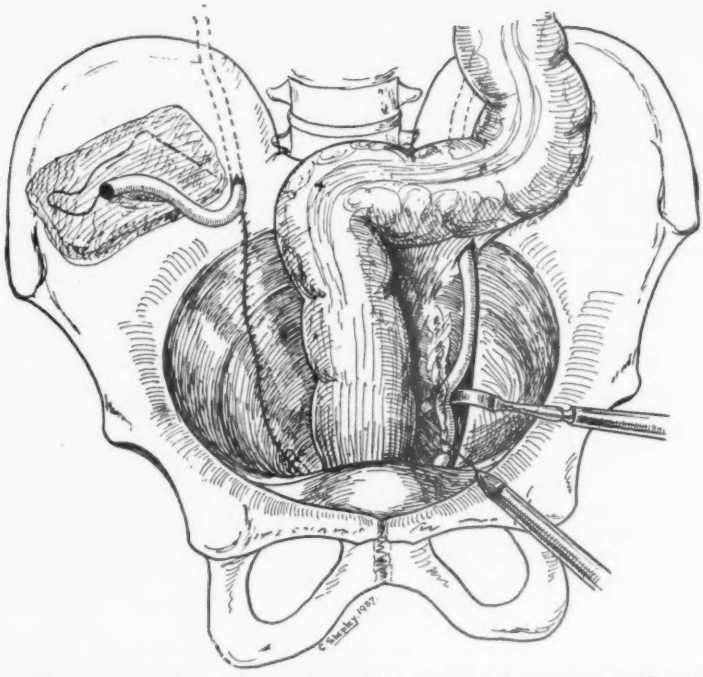

FIG. 6.—Technique of operation. Right ureter isolated, divided at its lower end, and prepared for implantation, and divided peritoneum sutured. Left ureter isolated below pelvic colon, ligatured at lower end, and in process of division by diathermy knife.

FIG. 7.—Technique of operation. Left ureter isolated below pelvic colon, displaced above colon and brought out through base of mesocolon, and prepared for implantation, peritoneum sutured.

beneath the mucous membrane of the bowel and projecting a short distance into the lumen of the channel. At the conclusion of this stage the ureters are seen traversing the peritoneal cavity for a varying distance before they enter the bowel; the shorter this passage the safer for the patient. At the same time the ureters must not be fixed and liable to tension. We therefore render the course of the ureters almost entirely extraperitoneal by suturing the bowel adjacent to the site of implantation to the parietal peritoneum at the point of the exit of the ureter, a tag of omentum on each side being used to fix the gut to the peritoneum (fig. 8). An important stage of the operation is now reached. It was introduced as the outcome of our first case of bilateral transplantation with continuous intravenous infusion. The immediate result of this treatment in this case appeared disappointing, and on the morning following the operation a tube was passed into the rectum when we were pleased, but frightened, to see a pint of limpid urine escape. Fortunately no damage was done

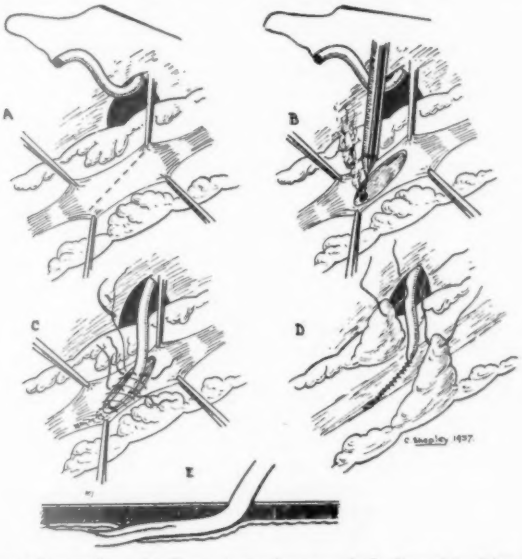

FIG. 8.—Technique of operation: (A) Preparing submucous bed; line of incision through serous and muscular coats. (B) Opening bowel with diathermy knife at distal end of submucous bed. (C) Ureter inserted, fixed and buried beneath serous and muscular coats. (D) Retroperitonealizing implanted ureter by uniting appendices epiploicæ to opening in parietal peritoneum at exit of ureter. (E) Scheme of implantation; formation of a mucous and nipple valve within lumen of bowel.

to the implantation, but in every case now we insert a tube into the rectum before the wound is closed, employing the method Lane used when doing an iliosigmoid anastomosis or a total colectomy. The hand of the surgeon low down in the pelvis guides a stomach-tube, which is inserted into the rectum; to this is attached a Higginson's syringe through which a jet of liquid paraffin is forced. The tube, having entered the rectum for a distance of three inches, is fixed by a suture to the thigh. The abdomen is now closed without drainage, and the patient returned to bed.

POST-OPERATIVE TREATMENT

The vitally important post-operative treatment demands an extremely high standard of nursing. Day and night, for the next ten days at least, the patient is constantly under supervision and frequently receiving skilled attention. The intravenous infusion apparatus is fitted up and into a vein in the arm a slow stream of sodium sulphate solution, followed by normal saline, flows. This is kept up for three

or four days, the amount administered being carefully regulated to prevent the patient becoming waterlogged. Usually by the evening of the day of the operation urine begins to flow through the rectal tube. By the use of a small dose of pituitrin ($\frac{1}{4}$ c.c.), repeated six-hourly if necessary, flatulent over-distension of the bowel is corrected. The rectal tube acts as a flatus tube and relieves distension greatly. It is often five or six days before it is wise to administer an aperient. Many other points require attention by the nursing sister at this stage, and others of importance arise later. Thus, for example, in those cases of intractable cystitis treated by ureteral transplantation, the now silent bladder may require to be washed out frequently. On the other hand, more than one case of this nature has not required any after-treatment to the bladder, which never appeared to give the slightest discomfort or produced the slightest inconvenience—a remarkable change when one remembers how just before the operation the urine was being painfully expelled about every half-hour. After about a fortnight, the patient begins to acquire what I may call " the habit of a functioning cloaca ", at first voiding urine two to three times during the night, but soon most patients go the whole night through undisturbed.

The nursing sister, to whom is due much of the credit in dealing with my cases, informs me that some of the women who have suffered much from frequency of micturition at first have a tendency to develop what I may call an irritable bowel, voiding urine unduly frequently from it. To correct this, tactful patient re-education is required before these patients also have undisturbed nights.

As I have mentioned, it was work done by my young colleague, Ian Lawson Dick, which led us to use sodium sulphate for intravenous injection as a post-operative diuretic in cases of ureteral transplantation. We consider that by its use we have eliminated the risk of post-operative anuria in these cases. We have referred elsewhere (*Edinburgh Medical Journal*, vol. **40**, 1934) to the experimental and clinical observations made, dealing with its use as a diuretic and the grounds on which its value as promoting renal secretion were based. All our subsequent experience since that article was written has gone to substantiate further the claims there made.

Ureteral transplantation on to the loins.—In the cases of vesical exclusion so far dealt with I have referred only to those in which the transplantation of the ureters into the colon, and the establishment of a cloaca thereby, was carried out.

Two other methods have been employed by me and are worthy of consideration, the first being that of transplanting the ureters on to the loins and creating there two fistulous openings through which urine is discharged. Such an operation is easy to do, safe and speedy, but has the great disadvantage that the collection of urine and the keeping of the patient dry are very difficult. So far we have not been able to devise any apparatus which worked with a reasonably constant efficiency when the patient was standing, sitting, or lying down. The operation cannot therefore be recommended merely on the grounds of enhancing the patient's comfort, and is only to be thought of as part of the treatment of malignant disease of the urinary bladder.

I have used it successfully as a preliminary to total cystectomy, but would now only adopt it if driven to this course by circumstances such as impaired renal function combined with gross dilatation of both ureters, rendering transplantation of the ureters into the colon inadvisable.

The possibility of the performance of this operation as a purely palliative procedure naturally occurs to one, when it is remembered how successful deviation of the intestinal flow is in the treatment of carcinoma of the rectum by a palliative colostomy. Unfortunately, such hopes are doomed to disappointment, which is particularly keen in the light of the terrible end of sufferers from vesical carcinoma. As the cancerous growth invades the bladder wall, there is painfully expelled a small quantity of foul-smelling, blood-stained urine, and this goes on day and night at intervals of a few minutes, and the patient, haggard with pain and want of sleep, clings precariously and almost unwillingly to a life of misery. After transplanting the ureters on to the loins in such a case, these spasmodic painful vesical contractions, unfortunately, still

persist, for it is not the urine that the bladder is endeavouring to expel, but the growth invading its wall. Thus the operation affords little relief as a palliative procedure. It is permissible, however, to do it as a palliative measure in a case of advanced carcinoma unsuitable for total cystectomy, and when combined with pre-sacral neurectomy, it produces appreciable relief.

Ureteral transplantation to natural fistulæ.—Another form of vesical exclusion that I have performed was in a man aged 53, who had had complete vesical exstrophy from birth and had more recently developed a carcinoma on the extruded bladder wall, which had remained untreated until it was very extensive. It had been in existence for two years and formed a foul-smelling large fungating growth ; in fact, to be candid, it was apparently more in the interests of the relatives than of the patient that the patient was transferred to my care.

Excretion urography examination showed a very extreme degree of dilatation of the ureters and renal pelves, obviously precluding the possibility of transplanting the ureters into the colon. Under ordinary circumstances this would have been scarcely possible. It was less so here, where it was first necessary to excise widely a large cancerous growth, a procedure necessitating the removal of a large portion of the entire wall of the lower abdomen. A method of vesical exclusion therefore was employed here similar in principle to that used by me in treating the ureter in a hemicystectomy for carcinoma of the urinary bladder. The ureters were divided and left undisturbed and allowed to form natural fistulæ where they lay. These fistulæ came, ultimately, after the bladder had been removed, to discharge on to the abdominal surface. The repair of the defect of the abdominal wall was successfully accomplished and to-day, twelve months after the operation, the patient is in good health, and the urine is voided into a depression on to the lower part of the abdomen, into which both ureters open.

In the cases of vesical exstrophy in the adult male that I have met with both testicles have been of full adult size and hanging over the pelvic brim below the spines of the pubis in separate large sacs.

Clinical examination and the patients' own statements have suggested that virility and potency existed. This has suggested to me the possibility of restoring the genital tract by a plastic operation after vesical exclusion has been performed, and the urine stream deviated into the bowel. I have one case that appears suitable for this treatment, and the patient is willing to submit to it, if I approve.

Statistics

I will now lay before you a brief statistical record of the 60 patients on whom I have operated during a period of fourteen years. You will note from the record, however, that the great majority of the operations have been done in recent years. You will also note that a large number of these patients have been sufferers from malignant disease of the bladder, either of primary or secondary origin. The mortality attending their treatment has been extremely high, and the reason for this is in part to be found in the critical state of the patients when they were operated on, for it is my belief—and will always be my practice to consider—that in the light of our present knowledge of the terrible distress that lies ahead for the patient suffering from malignant disease of the urinary bladder, we are fully justified in attempting any form of treatment, however heroic, that offers relief, or a possible cure. Earlier in this paper I have mentioned a fact which I would again dwell upon. It is that even where, clinically, the patients, although suffering from malignant disease, appear to be in sound general health, by test of renal function and other means of renal investigation, and the urinary tract is sound and free from infection, still in many of these cases they do not do well and are carried off, not by any unusual complication, not by any acute emergency arising, but by the slow sinking and absence of response that they show. As I said before, they would appear almost doomed to a fatal issue from the very onset. In dealing with them I have learned nothing that would make me incline to

modify the technique that we find so successful in certain of these cases and so constantly safe and sure in the non-malignant case.

From the detailed record of the 60 cases that I have treated and carried out the operation of vesical exclusion, four tables have been compiled.

TABLE I.

Transplanted to loin	5
Transplanted to fistulæ	1
Transplanted to bowel	
Two-stage operation	14
Single-stage operation	30
Single kidney	10

Since April 1934 in every case the operation has been performed in a single stage.

The five cases in which the ureters were transplanted on to the loins were operated on twelve and eleven years ago. Total cystectomy was subsequently carried out.

The single case described as transplanted to fistulæ has been referred to previously and was one of carcinoma developing in the extruded wall of vesical exstrophy.

In 54 cases the ureters were transplanted into the colon.

TABLE II.—POST-OPERATIVE MORTALITY.

	Cases	Deaths	Percentage
Transplantation of first ureter	12	5	45·5
Transplantation of second ureter	13	3	25
Transplantation of both ureters at same operation	36	15	40·5

In Table II the calculation of the post-operative mortality, according to the type of operation performed, is given. Under the category of transplantation of the first ureter are, of course, included all cases of single kidney.

TABLE III.—RESULTS OF WHOLE SERIES.

	Cases	Recoveries	Deaths
Non-malignant conditions	27	20	7 (25·5%)
Carcinoma	33	16	17 (51·6%)
Total ...	60	36	24

RESULTS SINCE JANUARY 1936.

	Cases	Recoveries	Deaths
Non-malignant conditions	11	10	1* (9%)
Carcinoma	14	8	6 (43%)
Total ...	25	18	7

* Cervical carcinoma treated by radium with formation of fistulæ from vagina into bladder and rectum.

In Table III the results since January 1936 are especially interesting. They illustrate the low mortality of the non-malignant conditions. This is especially noteworthy, particularly when it is borne in mind that the one case that was lost was a case of cervical carcinoma treated by radium, with subsequent formation of fistulæ extending from the vagina into the bladder and rectum. If the patient had recovered from the vesical exclusion, it was purposed to close the fistula in the rectum by obliterating the vagina and bladder.

The high mortality of cases of carcinoma has been already referred to.

TABLE IV.—ANALYTICAL RESULTS.

	Cases	Post-operative Mortality	Ultimate Mortality	Alive To-day
Vesical carcinoma	27	13	23	4
Vesico-vaginal fistulæ (obstetric injury) ...	9	0	0	9
Vesico-vaginal fistula (radium burn)	3	2	2	1
Persistent vesical systole (T.B.)	6	2	4	2
Congenital abnormalities	6	2	2	4
Urethral carcinoma	4	2	3	1
Intractable cystitis	3	0	0	3
Urethral stricture	2	2	2	0
Urethral fistula	1	1	1	0

In Table IV the high ultimate mortality of cases of vesical carcinoma is brought out. This is due to there being included those cases of carcinoma in which the patients died some many months or years after the operation, from the natural progress of the disease.